

# Sentinel surveillance of invasive bacterial vaccine-preventable diseases and rotavirus gastroenteritis

*Report of an intercountry workshop  
WHO Regional Office for South-East Asia,  
New Delhi, India, 20–21 June 2013*



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## Acronyms

ADIP	Accelerated Development and Introduction Plan
APW	agreement of performance of work
CSF	cerebrospinal fluid
DNA	deoxyribonucleic acid
DSH	Dhaka Shishu Hospital
ELISA	enzyme-linked immunosorbent assay
EPI	Expanded Programme on Immunization
EQA	external quality assurance
GFIMS	Global Framework for Immunization Monitoring and Surveillance
Hib	<i>Haemophilus influenzae</i> type b
IB-VPD	invasive bacterial vaccine-preventable diseases
ICMR	Indian Council of Medical Research
IPD	Invasive Pneumococcal Disease
NIP	national immunization programme
NUVs	New and under-utilized vaccines
PCR	polymerase chain reaction
PCV	pneumococcal conjugate vaccine
RRL	regional reference laboratories
RVGE	rotavirus gastroenteritis
SOPs	standard operating procedures
SSF	Shishu Shasthya Foundation
UK NEQAS	United Kingdom National External Quality Assessment Service
VPD	vaccine-preventable diseases
WHO	World Health Organization



# 1. Introduction

The six basic antigens of routine immunization provided through the Expanded Programme on Immunization (EPI) have prevented millions of vaccine-preventable diseases (VPD) globally since the 1970s. In addition, since 2000, opportunities have been available to provide benefits of new and underutilized vaccines, previously inaccessible and unaffordable in resource poor countries, to accelerate achieving Millennium Development Goal 4 with the support of the GAVI Alliance (formerly the Global Alliance for Vaccines and Immunisation). Although initiated with huge enthusiasm, the deployment of new vaccines in these countries has not been as rapid as anticipated due to a lack of epidemiological evidence for priority-setting and decision-making.

Having taken this constraint into consideration, the GAVI Alliance established Accelerated Development and Introduction Plans (ADIPs) to support the generation of evidence on disease burden and epidemiology of invasive bacterial vaccine-preventable diseases (IB-VPD) and rotavirus gastroenteritis (RVGE), for advocating to policy-makers and decision-makers on timely introduction of *Haemophilus influenzae* type b (Hib), pneumococcal and rotavirus vaccines into EPI. Operationalizing one key strategy of the ADIP projects in this direction, a hospital-based sentinel surveillance network with laboratory confirmation of cases was established to generate high-quality evidence.

In 2008, when the ADIP projects were discontinued, the World Health Organization (WHO) took over responsibility for coordinating the global IB-VPD and RVGE sentinel surveillance networks with continued GAVI financing, conditional to the subsequent transition of the networks to country ownership, country management and integration into existing VPD surveillance networks. However, to date, the IB-VPD and RVGE sentinel surveillance networks are technically coordinated and financially supported by WHO.

Despite WHO's active coordinating role, the current project-based approach to sentinel surveillance, exclusive dependence of the majority of sentinel sites on WHO/GAVI financial support, funding on an annual basis with substantial delays in fund disbursement, and significantly dwindling GAVI financial support are deemed unfavourable for the long-term sustainability of the IB-VPD and RVGE sentinel surveillance networks. Given that it will be impossible to abruptly abandon surveillance when the funding tails off, it is rational to explore the appropriateness and feasibility of the transition of managerial responsibility to countries and to gradually prepare the countries for imminent take over and integration of IB-VPD and RVGE surveillance into the existing VPD surveillance networks.

As regards the evolution of the IB-VPD and RVGE surveillance networks in the South-East Asia Region, the regional laboratory expertise and capacity in specimen collection, transportation and processing have improved significantly. On-site assessments have been carried out by experts from the Global Reference Laboratory and WHO, in Nepal and Sri Lanka as well in the two regional reference laboratories (RRLs) in Vellore, India, for IB-VPD and RVGE sentinel surveillance. These assessments have highlighted the need for further improvement in laboratory diagnosis and characterization of causative pathogens, standardizing laboratory practices/laboratory methods, and enhancing the capacity of laboratory staff in the network. Hence, it is considered timely and judicious to consult with the participating sites and agree upon how laboratory diagnosis and characterization of causative pathogens could be further improved, laboratory practices/laboratory methods could be standardized and the technical capacity of the staff could be further enhanced in the Region.

On-site assessments and review of data reported to the Regional Office for South-East Asia have also demonstrated some data quality issues related to both IB-VPD and RVGE surveillance in some sentinel sites. There is a need for all sentinel surveillance sites in the Region to generate high-quality surveillance (clinical, epidemiological and laboratory) data in a standardized manner and share with respective ministries of health, the Regional Office and WHO headquarters with a view to enabling national, regional and global policy-making related to IB-VPD and RVGE.

## **1.1 Objectives of the workshop**

### ***General objective***

The general objective of the workshop was to further strengthen sentinel surveillance of IB-VPD and RVGE to generate evidence on disease burden in the South-East Asia Region.

### ***Specific objectives***

The specific objectives of the workshop were:

- to explore mechanism/s for integration of IB-VPD and RVGE surveillance into the existing VPD surveillance network in the South-East Asia Region;
- to achieve consensus on implementing standard operating procedures (SOPs) for laboratory practices, enhancing national laboratory staff capacity and validating laboratory results;
- to discuss and agree on measures to improve quality and standardized reporting of surveillance data to ministries of health and WHO.

The Acting Director, Family Health and Research, inaugurated the workshop. Dr Shashi Khare, Additional Director and Head of the National Centre for Disease Control in New Delhi, India was chairperson. Professor Samir K Saha and Dr Shampa Saha of the Department of Microbiology of the Dhaka Shishu Hospital, Bangladesh were co-chairperson and rapporteur, respectively. Participants from 8 of the 11 Member States in the South-East Asia Region attended the workshop, including Member States that constitute the WHO-coordinated IB-VPD and RVGE sentinel surveillance network. The agenda and the list of participants are available in the Annex 1 and 2, respectively.

## **2. Proceedings of the intercountry workshop**

### **2.1 Global update on RVGE and IB-VPD surveillance**

The participants were provided with a global update on the status of IB-VPD and RVGE surveillance and use of vaccines against IB-VPD and RVGE. According to WHO estimates for 2008, 453 000 child deaths occurred due to RVGE and 82% of these deaths were in 20 countries. To date, 46 countries (24%) have introduced rotavirus vaccine in their national immunization programmes (NIPs). Another 12 (6%) and 15 (8%) countries plan its introduction in 2013 and 2014, respectively, while 121 countries (62%) have not introduced the vaccine.

Currently, there are 185 sentinel sites in 64 countries for RVGE surveillance that report data to WHO. Nearly 50 000 children were enrolled in 2012. In 2013, an external quality assurance (EQA) programme for laboratories was launched for all RVGE sentinel surveillance sites. WHO initiated efforts of partners to standardize genotyping of rotavirus strains in 2013. Consistency in surveillance practices over time is the key factor for assessment of the impact of rotavirus vaccination. For this purpose, preliminary criteria have already been established globally. These include establishing surveillance for RVGE, reporting of data at least one year prior to vaccine introduction, reporting data for at least ten months for each year, testing at least 100 stool specimens, non-zero reporting of tested specimens and monitoring of surveillance performance indicators.

In 2000, the global burden of IB-VPD was estimated at 14.5 million cases (uncertainty range 11–18 million) of which nearly 5.5 million cases (uncertainty range 4.3–6.8 million) were estimated to be in the South-East Asia Region. Global IB-VPD-specific deaths were estimated at 826 000 (uncertainty range 582 000–926 000) and the number attributable to the South-East Asia Region was 187 000 (uncertainty range 13 000–207 000). It was estimated that 91 000 deaths (uncertainty range 63 000–101 000) had occurred among HIV-positive patients. Ninety one countries (47%) have introduced the pneumococcal conjugate vaccine (PCV) into their NIPs. Twenty five countries (13%) plan to introduce PCV in 2013, while another seven countries (3.5%) intend to introduce it in 2014. The number of countries without PCV in their NIPs is 71 (36.5%).

In contrast to PCV, the Hib vaccine has already been introduced in 187 countries (96%). The number of countries that plan its introduction in 2013 and 2014 is three and two, respectively, leaving only two countries without use of Hib vaccine in the world.

Globally, 191 sentinel surveillance sites in 57 countries report data for IB-VPD to WHO. In 2012, these sentinel sites enrolled 22 516 children eligible for surveillance. The data pertinent to IB-VPD reported to WHO vary over time and across countries. In order to minimize the variability and improve the quality of data, WHO provides technical assistance, conducts sentinel site assessments and coordinates an EQA programme for the laboratory. It has also developed visual aids for improving clinical, laboratory and data management.

Summing up the global performance of the two networks since transition of their management to WHO, it was concluded that RVGE surveillance, being relatively robust, needed improvement in certain areas while IB-VPD surveillance required a fresh overall outlook.

In this session, participants were also familiarized with the recommendations of the Global New Vaccines Surveillance Meeting for Invasive Bacterial Vaccine Preventable Diseases (IB-VPD) held in Washington, DC, United States of America from 9 to 11 October 2012.

These recommendations were:

- characterization of surveillance sites to better understand the variability;
- seeking to include non-GAVI eligible countries in the IB-VPD network;
- communicating and publishing surveillance findings at all levels;
- measuring the impact of vaccines on IB-VPDs.

The recommendations to be implemented at the country level were:

- increased engagement of clinicians in the IB-VPD network through training and feedback;

- ensuring full involvement of national immunization technical advisory groups and encouraging them to generate advocacy;
- encouraging in-country advocacy activities such as:
  - sharing of surveillance data by the sentinel sites with the ministries of health with requests to generate advocacy;
  - advocating for establishing a government budget line for IB-VPD surveillance;
- developing annual country plans of actions for IB-VPD surveillance.

The specific funding criteria for the WHO-coordinated IB-VPD network, which would be implemented from 2013 with the aim of improving quality of surveillance, were:

- presence of a surveillance management team in each country that comprises a focal point from the ministry of health, each sentinel hospital, laboratory at the sentinel hospital and a focal point for data management;
- countries conducting only Tier 1 (meningitis) surveillance enrol at least 100 meningitis cases among children aged less than five years;
- data are reported regularly to WHO according to the schedule agreed upon with the Regional Office for South-East Asia;
- the hospital sentinel sites participate in the WHO's EQA programme for network laboratories;
- countries conducting only Tier 1 (meningitis) surveillance meet established quality indicators for Tier 1 before WHO provides funding for the country to establish Tier 2 (pneumonia-sepsis) surveillance.

The global update also included the outline of the proposed strategic review of the RVGE and IB-VPD surveillance networks. The strategic review was designed to determine whether the objectives of the two surveillance networks established in 2008 were achieved and, if achieved, the extent to

which objectives were met. The objectives of the two surveillance networks are:

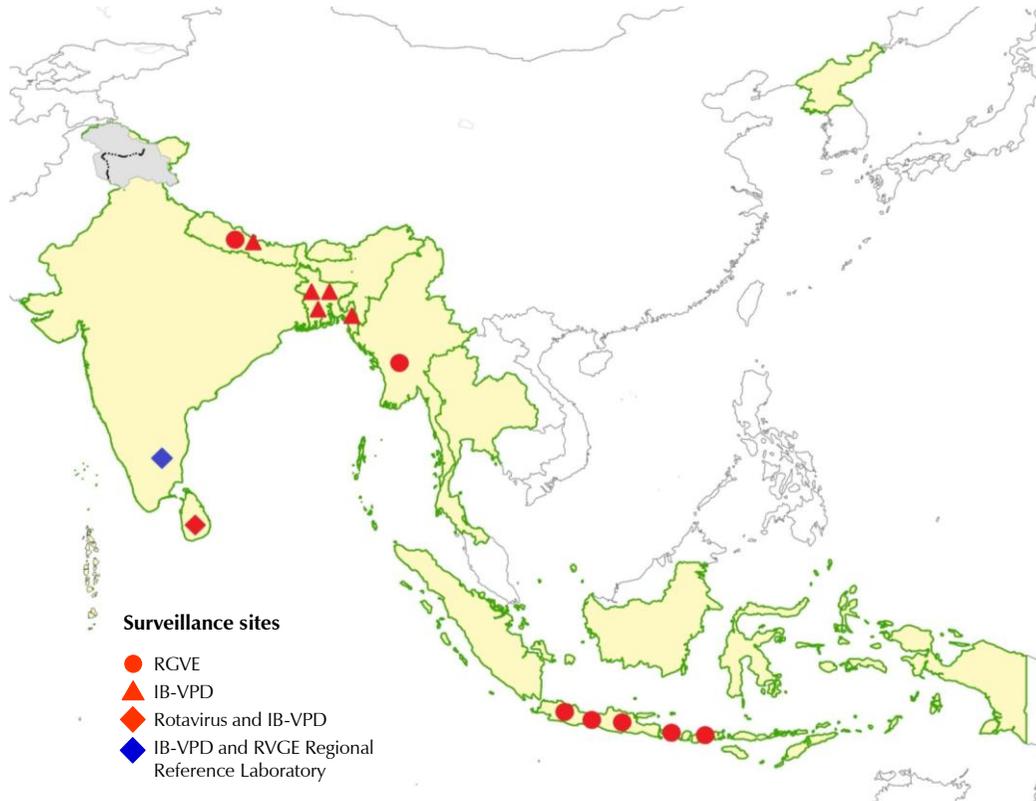
- generating data at the country level to confirm presence of disease, disease epidemiology and estimate disease burden;
- establishing systems to monitor the impact of introduction of new vaccines;
- establishing a system to monitor global serotypes and genotypes;
- monitoring antibiotic sensitivity.

The strategic review also intends to critically assess: the stance of the ministries of health on current IB-VPD and RVGE surveillance networks; the IB-VPD and RVGE laboratory surveillance network; capacity-building conducted in developing and maintaining these two networks; and management, generation, dissemination and use of data by the IB-VPD and RVGE surveillance networks. At the conclusion of the strategic review, it is expected to provide a future vision for the network. In this regard, the review will clarify the current objectives of the two networks including their contribution to vaccine impact assessment in the short and long term; determine the optimal strategies to meet these current objectives and overcome common challenges; define key indicators/milestones to monitor progress; and define potential complementary approaches to IB-VPD surveillance.

## **2.2 Regional update on RVGE and IB-VPD surveillance**

Currently, eight sentinel sites for RVGE surveillance exist in four countries in the Region, namely Indonesia, Myanmar, Nepal and Sri Lanka. For IB-VPD surveillance, five hospital-based sentinel sites and one population-based surveillance site exist in three countries, namely Bangladesh, Nepal and Sri Lanka. The RRLs for both IB-VPD and RVGE surveillance are situated in Vellore, Tamil Nadu, in India. The locations of the sentinel sites are depicted in Figure 1.

**Figure 1.** RVGE and IB-VPD surveillance network in the South-East Asia Region, 2013



For functionality of sites, logistics are procured in bulk by the WHO Regional Office for South-East Asia. However, delays in delivery sometimes occur due to difficulties in obtaining permission from country authorities to ship items. At times, providing specific branded items requested by sites is infeasible as they are not listed in the WHO's global management system. Another difficulty encountered by the Regional Office is its inability to provide country requirements beyond the given financial allocations, due to decreasing partner support for IB-VPD and RVGE surveillance.

Sentinel surveillance laboratories and national reference laboratories have enhanced their capacity in rotavirus detection by using enzyme immunoassays, and capacity in IB-VPD pathogen detection by using Gram stain, culture, and rapid diagnostic kits such as latex agglutination and

BinaxNOW *Streptococcus pneumoniae* antigen test. Sentinel surveillance laboratories and national reference laboratories have enhanced their capacity in molecular characterization of IB-VPD pathogens (e.g. Bangladesh) and genotyping of rotavirus strains (e.g. Indonesia and Myanmar). The RRL for IB-VPD surveillance enhanced its capacity in serotyping/serogrouping of IB-VPD pathogens by molecular methods with technical support from WHO and the Global Reference Laboratory. The RRL for RVGE surveillance provides genotyping services to the sentinel surveillance sites in the network, genotyping of non-typeable strains for Indonesia and Myanmar, and technical support to sentinel surveillance sites for the Government of India.

The sentinel surveillance laboratories/national reference laboratories for IB-VPD and RVGE have been participating in the global EQA programme since 2011 and 2013, respectively. The regional EQA programme has also been conducted until 2013, although it can be now discontinued given the participation of all sentinel sites in the global programme. Other regional achievements related to laboratory aspects include the development of regional RVGE surveillance SOPs for receipt, storage, and transportation of specimens to national and regional reference laboratories, and revision of the protocol for typing previously un-typeable samples.

The factors for low diagnostic yield of IB-VPD pathogens were also highlighted. Regional challenges include the high cost of despatching cerebrospinal fluid (CSF) specimens of all suspected meningitis cases to the RRL, complex technical demands (such as shipping in dry ice), and complexities around standard material transfer agreements. Taking into account the complex nature of these factors, measures aimed at strengthening molecular characterization capacity at the country level were suggested as probable solutions. In the meantime, WHO is developing global guidelines to prioritize the referral of samples from countries to the RRLs for both RVGE and IB-VPD surveillance.

All sentinel surveillance sites, as per agreement, share data with WHO. Nevertheless, given the need for standardized data from all sentinel sites in the network, compliance with the standard WHO aggregated data reporting format would be required from 2013 onwards.

The strengths and weaknesses of the two regional surveillance networks are summarized in Table 1.

*Table 1: Strengths and weaknesses of the IB-VPD and RVGE surveillance networks in the South-East Asia Region*

Strengths	Weaknesses
<ul style="list-style-type: none"> <li>• <b>Availability of a regional network for surveillance of IB-VPD and RVGE</b></li> <li>• <b>Availability of data prior to and after transition to WHO coordination</b></li> <li>• <b>Enhanced regional expertise in disease surveillance and laboratory aspects of IB-VPD and RVGE</b></li> <li>• <b>High performance of all sites in the WHO's formal EQA programme</b></li> <li>• <b>Establishing strong links with the Global Reference Laboratory and other global laboratories</b></li> <li>• <b>Availability of data related to the aetiological role of Hib, pneumococci and meningococci in IB-VPD, rotavirus in gastroenteritis and their strain characteristics</b></li> <li>• <b>Availability of stable data for periods required for technically substantiating vaccine introduction and post-introduction evaluations</b></li> <li>• <b>Opportunity for an integrated VPD surveillance network</b></li> <li>• <b>Availability of some data for country level decision-making</b></li> </ul>	<ul style="list-style-type: none"> <li>• Weak geographical representativeness of information generated, due to limited sentinel sites</li> <li>• Relatively suboptimal quality of IB-VPD data</li> <li>• Limited studies to quantify the burden of IB-VPD and RVGE</li> <li>• Varying degree of involvement of the ministry of health and EPI in sentinel surveillance</li> <li>• Varying degree of the expected quality of laboratory data, especially for IB-VPD</li> <li>• Non-integration into other in-country VPD surveillance networks</li> <li>• Availability of funds only on annual basis for surveillance</li> <li>• Project-based approach and financial dependence on WHO and other donors</li> <li>• Lack of involvement of WHO country offices in IB-VPD and RVGE surveillance</li> </ul>

Surveillance networks for both IB-VPD and RVGE offer many opportunities for further enhancing capacity of laboratory staff, post-vaccine introduction evaluations, and integrating data generated by sentinel

surveillance sites beyond the WHO-coordinated network. Moreover, the networks enabled building a more substantial evidence base than that which is currently available for decision-makers. The population-based surveillance site in Bangladesh was underscored as ideal to provide ample opportunities for operational research on IB-VPD in the Region. In addition, there is the opportunity to incorporate IB-VPD and RVGE surveillance into the existing VPD surveillance network in country-specific ways, such as possible use of in-country polio surveillance networks for rotavirus surveillance.

Despite the achievements, numerous threats have the potential to derail the gains of IB-VPD and RVGE surveillance in the Region. There is a real possibility of cessation of activities at some sites in the event of non-availability of funding through WHO. This raises the question of the future sustainability of surveillance if donors withdraw their financial support. A further threat is the rising unexpected costs incurred to some sentinel sites, due to administrative charges by hospitals where sentinel sites are located and taxations imposed on or lack of tax exemptions for logistics supplied for the programme.

## **2.3 Discussion on issues and challenges encountered by sentinel surveillance sites**

The countries involved in the WHO-coordinated IB-VPD and RVGE surveillance networks discussed the major challenges. The issues encountered are summarized below, by country.

### ***RVGE surveillance***

#### **Indonesia**

- Delayed confirmation of continued financial support by WHO for the impending financial year.
- Delayed receipt of instalments under the Agreement of Performance of Work (APW).
- Delays in sending samples to the RRL due to the prolonged period taken by the Ministry of Health to finalize the standard material transfer agreements.

- Delayed receipt of logistics (laboratory items) required for surveillance.
- Poor quality of some of the surveillance data collected.
- Infrequent feedback on data quality and inadequate reviews for improving data quality.
- Non-availability of SOPs for surveillance data sharing with in-country agencies.
- Delay in finalization of the final report on genotypes, due to late receipt of primers and other laboratory logistics.

### **Myanmar**

- Delays of 4–6 weeks between sending in the final technical report of completion of the work and receiving the final instalment.
- Delayed receipt of logistics procured by WHO.
- Receipt of some laboratory items without proper cold-chain maintenance.
- Polymerase chain reactions (PCR) with some primers; bands are not clear-cut.
- Inadequate amount of primers and enzymes for genotyping.
- Presence of still un-typeable strains among detected rotavirus strains.
- Inadequate time for processing EQA samples within the given deadline as a result of delayed delivery of EQA panels to Myanmar.
- Inadequate sharing of surveillance information with the Ministry of Health.

### **Nepal**

- Delayed receipt of logistics (laboratory items) required for surveillance.
- Lack of infrastructure for genotyping within the country.

- Inadequate sharing of surveillance information with other in-country agencies.
- Lack of a feedback mechanism on furnished data from WHO.
- Issues related to finding a courier system with standard cold-chain maintenance when sending specimens to the RRL.

## **Sri Lanka**

- Prolonged timeframe for finalization of the APWs by WHO, resulting in:
  - further delay in obtaining the approval of Ministry of Health for conducting surveillance;
  - inability to conduct surveillance from the beginning of the year;
  - delay in recruiting project staff, which is performed on an annual basis only after receiving the APW;
  - inability to continue surveillance throughout the year.
- Pre-intern medical graduates enrolled as research assistants join the internship in the middle of the year, affecting continuity of surveillance.
- Delay in receiving instalments.
- Inability to store faecal specimens before and after testing, due to lack of storage facility.
- Lack of adequate funding for specimen transportation to the RRL within the provided budget ceiling.

## ***IB-VPD surveillance***

### **Bangladesh**

- Delayed receipt of instalments under the APW.
- Issues related to collection, compilation, consolidation and interpretation of data, with changes in definitions of variables during the progress of the study.

- Lack of adequate financial resources for conducting post-introduction impact evaluation studies.

## **Nepal**

- Delayed confirmation of continued financial support from WHO for the oncoming financial year.
- Inadequacy of funds received through the APW for surveillance activities.
- Inadequate funding for dry ice to ship CSF samples to the RRL for strain characterization within the total funds allocated for surveillance by WHO.
- Difficulties in immediate, 24-hour plating of CSF.
- Non-compatibility of some definitions of surveillance with those used by other sentinel surveillance sites.
- Inadequate sensitivity of sepsis case definition for surveillance.

## **Sri Lanka**

- Prolonged timeframe for finalization of the APWs by WHO, resulting in:
  - further delay in obtaining the approval of Ministry of Health for conducting surveillance;
  - inability to conduct surveillance from the beginning of the year;
  - delay in recruiting project staff, which is performed on an annual basis only after receiving the APW;
  - inability to continue surveillance throughout the year.
- Pre-intern medical graduates enrolled as research assistants join the internship in the middle of the year, affecting continuity of surveillance.
- Delay in receiving instalments.
- Non-use of sheep blood for culturing IB-VPD pathogens at the sentinel surveillance site laboratory.

- Inadequate communication of data by publishing them for wider access.
- Inadequate two-way communication with the RRL.

## **2.4 Global experience of integrating IB-VPD and RVGE into VPD surveillance networks**

The changing context of disease control and prevention of VPDs was examined, including the:

- increasing programme costs with the increasing number of New and under-utilized vaccines (NUVs);
- increasing need for information to guide investments, reduce vaccine wastages, maximize impact of vaccines, and implement performance-based evidence;
- greater focus on monitoring and accountability frameworks, including that of the Global Vaccine Action Plan (GVAP), given that targets are no longer considered just aspirational targets;
- increased recognition of measurement of data variables and data quality as critical;
- varying disease epidemiology, and resultant varying surveillance objectives and needs for different VPDs;
- new technologies available for recording and reporting information and conducting surveillance;
- many parallel, uncoordinated approaches to using new technologies.

The significance of the Global Framework for Immunization Monitoring and Surveillance (GFIMS) was discussed within this changing context. The GFIMS outlines a vision for immunization monitoring and VPD surveillance, calls for integration of surveillance and monitoring systems, strengthens the capacity at country level, and emphasizes data quality assurance. The vision of the global immunization partners is a world benefiting from an integrated epidemiological, laboratory, and programme monitoring network dedicated to optimizing the surveillance for VPDs and monitoring of immunization programme performance. This network would provide the high-quality information needed to measure the impact of

vaccines and maximize their safe, effective and equitable use at country, regional and global levels to reduce or eliminate the burden of VPDs.

The global experience in integrating surveillance, existing types of surveillance, objectives and examples were shared. Maps of countries implementing case-based measles surveillance, rotavirus reference laboratories in the world, surveillance activity by WHO regions, PneumoADIP and Hib Initiative sponsored surveillance networks and paediatric surveillance networks in the WHO Africa Region were displayed.

Under the GFIMS, there is a need for bridging different types of sentinel surveillance and using research to obtain more comprehensive data. With regard to IB-VPD surveillance, the hierarchical surveillance levels range from Tier 1 (facility-based meningitis surveillance), via Tier 2 (facility-based pneumonia and sepsis surveillance) to Tier 3 (population-based surveillance). In addition to surveillance, pertinent research activities entail vaccine clinical trials and vaccine probe studies. It is not financially and operationally feasible to expect all sites to conduct all types of surveillance activity; hence, it was stressed that the suggested surveillance structure under GFIMS was a "tiered approach". In this tiered approach, Tier 1 comprises hospital sentinel sites for RVGE and IB-VPD surveillance. The normative standard for Tier 1 is one sentinel site per country (in larger countries up to three sites). Tier 2 includes additionally selected sites for pneumonia and/or sepsis surveillance. The normative standard is one site for every three countries. Tier 3 surveillance sites are population-based sites to generate incidence estimates. The normative standard for population-based surveillance is one surveillance site per WHO region. External to these tiered surveillance structures, there are centres of excellence that conduct specialized epidemiological studies to complement surveillance.

Participants were made aware of the current issues linked to surveillance. At present, multiple, vertical, disease-specific monitoring and surveillance is supported by over 100 global health partnerships. Some of these diseases are vaccine-preventable or potentially vaccine-preventable such as malaria, typhoid or dengue. Despite availability of surveillance data, there has been a difficulty in interpretation of data received through aggregated reporting. A significant amount of case-based data is required to overcome this problem. On the other hand, recording of data and data management systems are currently weak. Lack of information on reporting sensitivity, data quality and epidemiological data for review of policies on

"traditional" EPI diseases is also seen as a major gap. Complicating existing issues, surveillance for some diseases targeted by new vaccines is complex by nature. The complexities include performing invasive procedures such as lumbar punctures to collect specimens, timely transportation of specimens for conventional testing, and the need for a standard laboratory capacity that includes clinical, pathological tests and microbiology for testing samples. The non-availability of tests for establishing bacterial aetiology of pneumonia was also highlighted as an impediment for effective surveillance.

There is a renewed interest in monitoring and evaluation of VPDs triggered by factors such as the GVAP Monitoring and Evaluation/Accountability Framework, the attention of major donors (GAVI Alliance, Bill and Melinda Gates Foundation, Centers for Disease Control and prevention (CDC), etc.), increased availability and use of information and communication technologies, and progress achieved in enhancing VPD surveillance platforms. Within this context, it is appropriate to consider activities to integrate VPD surveillance. Building on existing platforms for surveillance and synergizing surveillance efforts are critical steps. In addition, the appraisal of surveillance data quality ensures improved utility of aggregated VPD data reports. Scaling-up of VPD surveillance would also enable the exploring of new diagnostics (particularly for IB-VPD); improve data management systems and data sharing; provide better tools for using surveillance data to estimate burden and monitor impact; and expand outbreak investigation using the measles/rubella platform. Surveillance could also be a means to explore alternate methods for assessing the impact of PCV using pneumonia or nasopharyngeal carriage as outcomes. Hence, there is a need for advocating for investments in VPD surveillance and monitoring at all levels. In terms of establishing partnerships and collaborations, the need to channel investments from different global initiatives into an integrated system (disease-specific to objective-oriented) exists.

In conclusion, citing global experience in the integration of VPD surveillance, it was underscored that transition takes time and requires discussion and meticulous planning. Similarly, the involvement of the ministries of health is deemed critical. Global experience also highlights the importance of data sharing by sentinel surveillance sites, data ownership, supportive supervision, and the involvement of national technical advisory groups on immunization.

## 2.5 Global laboratory update on IB-VPD surveillance and expected regional standards

The objectives of the global IB-VPD laboratory network are (a) supporting surveillance networks and evidence-based decision-making on vaccine introduction and use, (b) assisting countries in establishing well-functioning laboratories with adequate quality assurance systems, (c) providing reliable, accurate and timely information, and (d) monitoring distribution of serotype/serogroups of pathogens causing IB-VPD (*Streptococcus pneumoniae*, Hib and *Neisseria meningitidis*).

An update on global activities was presented. In 2012, the IB-VPD laboratory technical working group was convened, comprising selected technical experts in clinical bacteriology and disease surveillance, WHO coordinators, and global and regional reference laboratory coordinators. The objectives of the working group are to provide WHO with technical guidance to strengthen bacteriological laboratory capacities related to the isolation, identification, serotyping/serogrouping of *S. pneumoniae*, Hib and *N. meningitidis* within the IB-VPD network, and to improve the overall quality of both laboratory and epidemiological data collected through the IB-VPD surveillance network. In order to optimize laboratory procedures, the following activities have been performed: recommending procedures for diagnosis at sentinel surveillance hospital laboratories; adding a rapid diagnosis test at the sentinel surveillance sites level; and sending isolates and CSF samples to RRLs for characterization and serotyping/serogrouping by PCR.

Another important area highlighted was the EQA programme. The laboratory coordinator for IB-VPD surveillance from WHO headquarters explained the EQA procedure and shared the results of the laboratories' performance. Problems identified included the non-response of nearly 22% of participants, late submission of results, and poorly completed and submitted forms. In order to improve the process, root-cause analysis, problem-solving and gap analysis were required. Based on this analysis, developing national plans for corrective and preventive actions was recommended as an essential activity.

The presentation next dealt with recommendations from the Global new vaccines surveillance meeting for IB-VPDs held in October 2012. The

laboratory-specific recommendations were: (i) advocacy for clinicians to increase the volume of CSF within the network and rationale for lumbar puncture; (ii) summarizing the agreed algorithm on priority testing of CSF at sentinel site laboratories; (iii) implementing a more challenging EQA programme for RRLs; (iv) and exploring antimicrobial activities in CSF at RRLs. The presentation also focused on recommendations for priority testing when the volume of CSF was more/less than 1 ml.

Optimization of deoxyribonucleic acid (DNA) extraction and PCR procedures for the RRLs were also discussed. Standardization of PCR procedures would allow some regional flexibility, so long as results were acceptable to the network. A further aspect of this is the quality control procedure for confirmatory testing between RRLs and the Global Reference Laboratory. With regard to data reporting, there is a need for standardization of reporting formats for sentinel surveillance sites and RRLs, for better linkage of clinical and laboratory data. The RRLs were requested to be cautious when reporting data back to WHO. The network faced multiple challenges, including dealing with large numbers of cases with prior antibiotic use, high numbers of culture-negative cases, and sentinel surveillance sites using human blood in their laboratories (instead of more appropriate sheep or horse blood). Other major challenges were the transporting of CSF specimens and processing them within an hour after collection, staff training, ensuring logistics, communication, resources for storage and transport of specimens to RRLs, sustainability of laboratory supplies, analysis of data with provision of a feedback and maintaining the cycle between laboratory and clinicians.

From the regional perspective, it was essential to list the regional expectations so as to enable participants to implement essential requirements to improve laboratory diagnostics of IB-VPD pathogens. One expectation was to apply recommended global guidelines. To achieve this, it is required to train laboratory personnel on recommended procedures (Gram stain, culture and rapid diagnostic tests). Regional workshops and on-site visits may act as suitable platforms to provide these trainings. Continuous communication between sentinel sites, the RRL and the WHO Regional Office for South-East Asia are vital for problem-solving, data analysis and ensuring availability of adequate laboratory supplies. WHO needs to assess the capacity of the RRL in providing necessary assistance to countries in the Region. Participation in the EQA programme helps

laboratories identify areas where more focus is required and implement corrective actions.

In conclusion, surveillance for IB-VPD requires improvement and greater consistency than it has at present. The Region has to develop SOPs for IB-VPD surveillance, based on global guidelines, for implementation at the regional or country level. Shedding light on the pending global strategic review, the presentation underlined that the proposed review would be critical to outline next steps. These steps include (i) deciding if the original objectives of the laboratory network have been met (ii) defining roles and responsibilities of different stakeholders and (iii) determining the added value of recommended tests, namely PCR and BinaxNOW.

## **2.6 Global laboratory update on RVGE surveillance and expected regional standards**

Participants were presented with an overview of the global RVGE surveillance laboratory network and an update on activities performed. The laboratory technical working group for the WHO rotavirus surveillance network, met in Bangkok in 2012, had revised the use of "common" and "uncommon" rotavirus strains, and recommended five globally common strains based on available reviews (G1P[8], G2P[4], G3P[8], G4P[8] and G9P[8]). In spite of this, reporting of regionally common or emerging strains has been promoted and the reporting form had been adapted to allow reporting all G and P combinations. This has facilitated highlighting the top 5–10 prevalent genotypes globally, and in a particular region, per year. Global surveillance data as reported in the Global Rotavirus Information and Surveillance Bulletin in 2011 was shared with participants.

It was highlighted that genotyping protocols to decrease the non-typeables had been updated. The Qiagen OneStep kit for the first round reverse-transcription (RT) PCR was reported to have been more sensitive and robust than the previously used protocol. Although the kits have been included in the WHO catalogue system, the high price is unaffordable for many laboratories. Hence, there is a need for more studies on cost-effectiveness and comparison of different protocols and less expensive kits. The need for harmonizing the primer sets used was also discussed.

In coordination with the Global Reference Laboratory, a global EQA programme is in operation for the RVGE surveillance laboratory network. Individual laboratories are sent unknown specimens in proficiency testing panels for antigen detection and genotyping assays, where applicable. Proficiency testing allows laboratories to regularly evaluate their performance and improve the accuracy of their results. Each participating laboratory receives feedback on their performance, as well as a report summarizing the results of all participating laboratories.

For the 2012 EQA programme, panels were prepared by CDC, Atlanta, by diluting specific genotypes into an artificial stool matrix. It consisted of eight rotavirus-positive and -negative samples. Common G types and P types were represented in the panel. The panels were prepared, quality controlled, stored in freezers, and shipped on dry ice. In addition to the high shipping cost, shipping on dry ice restricted the despatching of panels to all participatory laboratories in the RVGE surveillance network. The sample quality became too degraded after prolonged storage at 4°C or higher temperatures. In contrast to 2012, the lyophilized sample format used in 2013 increased temperature stability and the ability to be stored at the ambient temperature. It also greatly reduced the shipping costs, from an average cost of US\$ 1796 in 2012 to US\$ 100 in 2013. In 2012, panels had been shipped to 45 laboratories while in 2013 the number had increased to 136 laboratories. How RRLs, provincial and national laboratories in the network performed on enzyme immunoassays and genotyping was shared with the participants.

In conclusion, the overall recommendations of the laboratory technical working group for the WHO rotavirus surveillance network were shared with the participants. The working group had recommended improving the quality of genotyping. For these purposes, the recommendations of the technical working group in 2012 called for consensus on laboratory procedures; approaches to decrease non-typeable strains; developing quality control guidelines for confirmatory testing between RRLs and the global reference laboratory; referring non-typeable strains by countries to the RRLs for genotyping and sequencing; and developing guidelines to standardize strain characterization. Other recommendations were to hold regular meetings, at least annually, between countries and RRLs; and to prepare regional SOPs, including for specimen collection and transport, and to implement them and update them when necessary.

## **2.7 RRL update on rotavirus surveillance: issues and challenges**

The Wellcome Trust Research Laboratory in Vellore, India, has been working in the area of rotaviruses since 1976. The laboratory introduced molecular methods in the mid-1990s. In 2010, it was designated as the RRL to provide services to India, Indonesia, Myanmar, Nepal and Sri Lanka. These services include routine genotyping, genotyping of un-typeable strains, training, and quality assurance. Several methods are available at the RRL for screening rotaviruses and strain characterization; however, the methods of choice are enzyme-linked immunosorbent assay (ELISA) for detecting VP6 antigen and RT-PCR for VP7 and VP4 genes.

For the regionally conducted EQA, each sentinel surveillance laboratory or national reference laboratory was provided with a pack of 10 samples annually for screening and, if need be, for genotyping. Results were submitted to the RRL within four weeks of receiving samples. If any laboratory had a performance level of less than 80%, or less than 90% on two occasions, they would be provided with training and help to troubleshoot the assays. The last shipment was carried out in January and February 2012. Given that WHO headquarters has initiated a formal EQA programme with the “easy to deliver” lyophilized proficiency testing panels, the need for conducting the regional EQA no longer exists. As regards genotyping, the RRL provides quality checks for genotyping results in testing panels, reference services for network laboratories performing typing of strains as yet un-typeable, and reference services for genotyping of un-typeable samples.

The results of genotypes from Indonesia, Myanmar, Nepal and Sri Lanka were discussed. It was noted that the highest rate of mixed infections was found in Nepal (15%). The proportion of globally common strains (G1P[8], G2P[4], G9P[8]) was 97% among characterized strains in Sri Lanka, 43% in Myanmar and 28% in Nepal. G12 strains were found in all sites. They were the predominant strains in Myanmar and Nepal and were seen in combination with P[6] and P[8]. G9 was seen in combination with P[4] and P[6] in these two countries .

Although available data were limited, they showed remarkable strain differences in countries of the South-East Asia Region. These data have to be interpreted with caution, given the small number of countries involved in surveillance and the fact that the small number of samples collected from

the Region is intended to be roughly representative of a very large proportion of the global population. The other challenge that the WHO RVGE surveillance network has to address is better timing of contracts, shipment of reagents and samples to the RRL.

## **2.8 RRL update on IB-VPD surveillance: issues and challenges**

The RRL provides services to Nepal and Sri Lanka in the WHO-coordinated IB-VPD surveillance network and to 11 participating centres in the surveillance network of the Indian Council of Medical Research (ICMR). In addition to the services provided to laboratories in the WHO network, the RRL conducted training workshops for the ICMR participating centres, shared manuals and posters prepared by WHO and introduced BinaxNOW tests. In terms of capacity strengthening of the RRL, the Global Reference Laboratory at CDC conducted a follow-up training workshop in June 2012. The RRL has acquired the capacity to detect IB-VPD and conduct pneumococcal serotyping by molecular methods. The “RNase P PCR method” has also been introduced.

The RRL receives isolates of *S. pneumoniae*, *N. meningitides*, Hib and CSF samples from the sentinel surveillance laboratories or national reference laboratories. Isolates are reconfirmed at the RRL. Subsequently, the serotype is determined, anti-microbial susceptibility is defined, and isolates are stored. The RRL performs real-time PCR on CSF samples to identify *S. pneumoniae*, *N. meningitidis* and Hib. The results of three major IB-VPD pathogens determined from the samples received by the RRL, serotype distribution, and antimicrobial susceptibility of *S. pneumoniae* were displayed in the workshop.

The RRL participated in the WHO-coordinated EQA programme conducted by the National Institute for Communicable Diseases, South Africa, and United Kingdom National External Quality Assessment Service (UK NEQAS). In 2011 and 2012, the RRL performed exceptionally well by scoring 100% three times and 95% in four assessments. The RRL participated in the assessment conducted in 2013 by UK NEQAS and results are expected. The results of the EQA conducted by the RRL for Nepal and Sri Lanka were also discussed. Both laboratories had obtained marks well above the satisfactory level, which was 75%.

The RRL for IB-VPD surveillance, however, continues to face issues and challenges, including:

- a high proportion of un-typeable serotypes of *S. pneumoniae*;
- the need for training in molecular techniques to detect organisms directly from the specimens and to detect positives from culture-negative samples
- the non-availability of good blood agar plates
- fulfilling a re-induction training request from Nepal and Sri Lanka for their laboratory staff;
- receiving culture-negative CSF specimens from Nepal and Sri Lanka for molecular characterization by PCR;
- obtaining permission of the Sri Lanka government for receiving CSF specimens;
- high costs for dry ice shipping of CSF specimens;
- the need for to consider sending DNA extracts to the RRL.

Discussions focused on possible solutions to issues in the shipment of culture-negative CSF specimens from Nepal and Sri Lanka.

## **2.9 Discussion on feasibility of implementation of regional SOPs on rotavirus laboratory practices**

This session focused on achieving consensus on the implementation of regional SOPs for rotavirus laboratory practices. The SOPs include (i) receipt and storage of faecal specimens at the sentinel surveillance hospital laboratory if this same laboratory performs ELISA to detect rotaviruses, (ii) receipt and storage of faecal specimens at national or central laboratories if the sentinel surveillance hospital laboratory does not perform rotavirus identification and (iii) specimen transfer within and outside the country for antigen detection, genotyping and quality assessment. Additionally, it was expected to assess the feasibility of using the study manual for RVGE prepared by the RRL (for use by sentinel sites coordinated by the ICMR) as a guiding document for developing national study manuals in participating countries of the WHO-coordinated RVGE surveillance network.

Country laboratory coordinators highlighted aspects of SOPs that were difficult to implement in local settings. The WHO headquarters laboratory coordinator, colleagues from the RRL, and other country participants shared experiences with a view to enabling learning from each other. Laboratory coordinators of RVGE surveillance in the regional network agreed to formulate the meeting recommendation on implementing regional SOPs on laboratory practices in the South-East Asia Region. Clarification was sought regarding the need for shipping materials using the basic triple-packaging system and also the need for adding glycerol. The rationale for these SOPs and their global application were discussed, and the WHO headquarters laboratory coordinator agreed to further discuss the need for the triple-packaging system versus double-packaging with global experts, and convey their opinion back to the Regional Office for South-East Asia.

Consensus was achieved that all participating countries in the WHO-coordinated RVGE surveillance network will implement the regional SOPs, with modifications suitable to the local setting. It was also agreed that the Regional Office would coordinate preparing a similar set of regional SOPs for IB-VPD surveillance by the RRL, and then share them with the country and WHO laboratory coordinators for their comments before adoption by the laboratories in the regional IB-VPD surveillance network.

## **2.10 Planning for post-introduction impact evaluation of pneumococcal vaccine in Bangladesh**

Bangladesh is well ahead of time in achieving Millennium Development Goals 1, 4 and 5, as quoted in national and international media reports. Multiple modalities of IB-VPD surveillance exist in Bangladesh. These include (i) the network of multiple sentinel surveillance hospitals in urban and rural Bangladesh (ii) the nested, urban, population-based surveillance around sentinel surveillance sites in Dhaka and (iii) the rural, population-based, active surveillance in Mirzapur. All modalities of surveillance are linked to hospitals. The modalities are designed to provide services for patient care which also motivate the clinicians to collect and send specimens to respective laboratories. The Bangladesh IB-VPD surveillance network consists of four hospitals in urban and rural Bangladesh with 1 105 paediatric beds and 36 536 yearly admissions. The surveillance team has access to all patients aged under five years and laboratory specimens in network hospitals.

The population-based rural surveillance site includes a hospital with 750 beds and laboratory facilities. Its catchment area is larger than that of the urban IPD surveillance site. In this area, with a child mortality rate of 53 deaths per 1000 live births, each child is visited weekly by a family health worker.

A post-introduction impact evaluation study of pneumococcal vaccine is planned for Dhaka. The city has a population of 16 623 000; the population aged under five years accounts for 759 409. The study will be carried out in one sentinel surveillance site with two high-performing hospitals, namely Dhaka Shishu Hospital (DSH) and Shishu Shasthya Foundation (SSF). These hospitals in the sentinel surveillance site are the only dedicated paediatric hospitals in the city and about 45% of children are treated free of cost (without insurance). Although patients come from throughout the country, the majority of service users are from Dhaka city. With 770 beds and 26 209 admissions per year, 97 invasive pneumococcal diseases (IPD) are detected at these two hospitals annually. The selection of the two hospitals for the impact evaluation study was based on (i) their close proximity (ii) use of the same laboratory facility (iii) ability for clinical management by rotating the same study team and (iv) ability to consider the two hospitals as a single surveillance entity.

The number of meningitis cases seeking care at the two hospitals is expected to be high. Their home locations would be recorded. The “catchment area” will be defined as the area from where most of the cases will be recorded. The population of the catchment area will be known and hence, the known denominator will facilitate calculating the incidence rates of the IPD. To determine the denominator, a yearly population census along with an assessment of health-seeking behaviour will be carried out. Based on the census, the population in the catchment area will be multiplied by the proportion of the population utilizing services of the two target hospitals. The selected catchment area reflects a typical urban population that consists of both slums and non-slums. The numerator will be the IPD patients identified at the two hospitals of the sentinel surveillance site. Incidence of IPD will be determined using the formula given below:

**Number of new cases of the disease (IPD) during the period “X”**

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**Catchment population × proportion utilizing services**

Epidemiological models determining the impact of Hib vaccine on disease incidence indicate that the evidence from the population-based surveillance and sentinel site surveillance produced similar results.

Over the years, the diagnostic yield of pneumococci has been vastly improved by better diagnostics in sentinel surveillance sites in Bangladesh. A wealth of surveillance information over a long time period is available on age distribution of IPD, cumulative IPD cases in children aged under five, detected serotypes, and cumulative IPD cases positive for 10-valent PCV (PCV-10) specific serotypes among children aged under five.

As regards the data from the nested, urban catchment area, incidence rates are available for suspected, probable, purulent and pneumococcal meningitis. The proportion of pneumococcal serotypes included in PCV-10 among all pneumococcal serotypes determined in meningitis cases (vaccine serotype coverage) in the catchment area and the sentinel surveillance site was 43% and 44%, respectively. The overall proportion of IPD cases attributable to serotypes included in PCV-10 was 45%. This is much lower than in other countries, specifically in the developed world.

At present, Bangladesh has decided to introduce PCV-10. The next step should be measuring the impact of PCV-10 on IPD in Bangladesh. This assessment requires availing quality data of the pre-vaccination period for multiple years and also considering the low coverage of pneumococcal serotypes included in the PCV due to diverse Bangladesh-specific invasive pneumococcal serotypes. Available data indicate that if PCV-10 is introduced, serotypes in PCV-10 cover 44% of pneumococcal serotypes among meningitis, 47% among non-meningitis and 45% among all IPD in Bangladesh.

The plan for assessment of the impact of PCV-10 in Bangladesh is as follows.

- To continue surveillance at the sentinel surveillance site (two hospitals: DSH and SSF) in Dhaka and compare pre- and post-vaccination data with rigorous collection of vaccination history:
  - conducting primary analysis of PCV-10-specific IPD cases;
  - conducting secondary analysis of all IPD cases.

- To conduct an analysis of “before and after” case series (as suggested by Hampton et al)<sup>1</sup> at the two hospitals of the sentinel surveillance site in Dhaka
- Calculation of incidence of the disease at population-based sites:
  - incidence rates of meningitis in the urban, nested population-based site (DSH-SSF). The analysis will include meningitis caused by vaccine serotypes, all pneumococcal meningitis, and probable and purulent meningitis cases;
  - incidence rates of meningitis in the rural, population based sites (Mirzapur). This analysis will include calculating incidence rates of IPD caused by PCV-10 serotypes and all IPD cases.

The other area for focus will be the impact of the vaccination on pneumococcal carriage. A comparison of data pertinent to invasive and carriage strains in Bangladesh was presented. Available data also allow Bangladesh to look at the impact of PCV on disability at the sentinel and population-based surveillance sites. At the former, there are about 64 cases per year while the incidence at the population-based site is estimated to be 50 per 100 000 child years. Among meningitis cases, 45% of survived cases have single or multiple types of disabilities. Given the burden of disease and disabilities in a birth cohort of about 4 million, the impact of PCV on IPD is expected to be enormous in Bangladesh.

Conservative estimates of the expected impact of PCV-10 on vaccine-type IPD (caused by serotypes included in the PCV-10) and overall IPD in Bangladesh were demonstrated. Based on these data, despite the low coverage of serotypes circulating in Bangladesh by PCV-10, it will have a remarkable impact on reduction of child morbidity and mortality. However, it has been cautioned that there could be an emergence of non-vaccine serotypes in the post-introduction period.

Research activities are moving fast at the global level and a new generation of vaccines are expected to arrive in the next few years. However, given the fact that children are dying every day, Bangladesh stressed that it could no longer wait for vaccines in the pipeline. The impact

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<sup>1</sup> Hampton LM et al. Sentinel versus population-based surveillance of pneumococcal conjugate vaccine effectiveness. *Bulletin of the World Health Organization*, 2012, 90:568–577.

of PCV on IPD has been established as a global public health triumph. If the same vaccine is used in Bangladesh, or in any other country with a large birth cohort and a high disease burden, the impact would be enormous. The anticipated impact in Bangladesh based on calculations using the disease burden data derived from the global estimates (O'Brien KL et al, 2009)<sup>2</sup>. was demonstrated.

In summary, the urban, nested population-based surveillance with known denominators allows calculation of incidence rates of meningitis. The rural population-based surveillance site has a relatively low number of isolates. However, measuring impact in a rural area is deemed important, as about 77% of Bangladesh's population live in rural areas. This site is also important given that most of its pneumococcal isolates are from cases of pneumonia/sepsis in contrast to the urban sites, where the majority of pneumococcal isolates are derived from meningitis.

## **2.11 Standardized data reporting and quality of data: global expectations**

Global expectations on data quality and standardization of data reporting within the WHO-coordinated IB-VPD surveillance network were shared. The globally accepted case definitions for Tier 1 meningitis surveillance and Tier 2 pneumonia/sepsis surveillance were presented. Similarly, definitions of suspected and confirmed rotavirus cases recommended by the WHO-coordinated RVGE network were shared.

The next focus was on surveillance performance indicators used by both WHO IB-VPD and RVGE surveillance networks. The global targets and the regional targets (that have yet to be determined) were discussed. How participating countries around the world met the targets in 2009, 2010 and 2011 were demonstrated for selected indicators. In order to ensure that sentinel sites complied with all global requirements in data management, participants were familiarized with the global expectations. In this regard, the importance of sharing data equally with WHO and respective ministries of health was stressed.

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<sup>2</sup> O'Brien KL et al. Burden of disease caused by *Streptococcus pneumoniae* in children younger than 5 years: global estimates. *Lancet*, 2009, 374:893–902.)

Consistent data management is the critical element for standardizing VPD sentinel surveillance. In order to ensure consistency across the WHO-coordinated surveillance network, clinical and laboratory posters and data management pamphlets have been developed by WHO including the “Data Management and Analysis Tips for IB-VPD Surveillance” pamphlet. The core areas detailed are: gathering and recording data, core data variables, data entry, checking data quality, analysing data with examples of data analysis, reporting, and ensuring data security. The other important area focused on was the WHO reporting template that had to be complied by all sentinel sites when they reported data to WHO. The requirement of timely, standardized reporting of data on the WHO data template, which included key variables for data sharing consensually agreed upon in the meeting of standardization of data in 2008, was emphasized.

In conclusion, the importance of adhering to SOPs, consistency, using the data management pamphlet which outlines a process for data management that is useful for both rotavirus and IB-VPD surveillance, using surveillance indicators to monitor surveillance performance and changes over time, critical nature of local knowledge for enhancing the sensitivity and the need for cautious interpretation of generated data were highlighted.

## **2.12 Discussion on measures to improve quality and standardized reporting of surveillance data to ministries of health and WHO**

The following areas were discussed with a view to improving standardized reporting of surveillance data and reporting quality data to WHO and respective ministries of health.

**Issues with surveillance case definitions pertinent to IB-VPD; in particular, the case definition for sepsis:** Issues encountered due to the inadequate sensitivity of the sepsis case definition were discussed. It was agreed that it would have to be looked at WHO headquarter level, in a technical working group discussion.

**Sharing case-based data for IB-VPD:** Currently, the South-East Asia Region does not share case-based information with WHO headquarters. The willingness of sharing case-based data has to be ascertained from the

principal investigators of sentinel surveillance sites. Hence, following the strategic review, WHO headquarters will identify the core variables of data for case-based surveillance and inform the Regional Office for South-East Asia. The Regional Office will obtain the opinion of the principal investigators in this regard and inform WHO headquarters. It was also stressed that publication policy has to be clear cut when case-based data is collected from the sentinel surveillance sites.

**Web-based data:** The feasibility of web-based databases as an alternative to excel spread sheets, and related issues, was discussed.

**Practical issues related to data reporting from sentinel surveillance sites on current WHO reporting forms:** Issues were highlighted (excluding reporting outpatient data, inability to report population-based surveillance data in current formats, etc.) and feasible solutions were discussed. Participants agreed to standardize current WHO reporting formats.

**Reporting on non-standardized reporting formats:** There is a need for a standardized reporting format when samples are sent to the RRL from sentinel site/national laboratories, and for standardized feedback of results from the RRL to WHO and sentinel site/national laboratories. WHO headquarters agreed to share a standardized format for implementation.

### **2.13 Establishment of step-wise mechanism/s to integrate RVGE and IB-VPD surveillance into the VPD network in the South-East Asia Region: outcome of the group discussion**

The group discussion explored step-wise mechanism/s for integration of IB-VPD and RVGE surveillance into the existing VPD surveillance networks in Member States in the Region. The discussion involved participants from the WHO-coordinated RVGE and IB-VPD surveillance networks, those representing other networks such as the governments of Bangladesh and India, as well as participants from Maldives and Thailand. Participants representing RVGE and IB-VPD surveillance networks discussed step-wise mechanisms separately in a brainstorming session. At the end, the two groups presented the mechanism/s agreed upon by the group members. The meeting recommendations include the suggested mechanisms for integration to be considered by WHO. The conceptual framework used for the discussion is given in Annex 3.

### **RVGE surveillance**

The first step in step-wise integration of RVGE surveillance into the existing VPD surveillance networks is voluntary sharing of surveillance information with the relevant department or unit in the respective ministries of health on a quarterly basis. For those countries that are not members of the WHO-coordinated RVGE surveillance network, the group suggested sharing surveillance information with WHO on a voluntary basis subject to the concurrence of the national surveillance network coordinators. In order to ensure prompt actions in this regard, the group analysed the current status of integration of RVGE sentinel surveillance sites into the existing national disease surveillance networks by sharing data/information generated by sentinel sites in participating countries. The current status is given in Table 2.

*Table 2. Current status of integration of RVGE surveillance with VPD surveillance networks (by sharing of surveillance data/information)*

<b>Country</b>	<b>Network</b>	<b>Sharing data with ministry of health</b>	<b>Sharing data with WHO</b>
<b>Bangladesh</b>	IEDCR	Yes (bi-annually)	No
<b>Indonesia</b>	WHO network	Yes (annually)	Yes
<b>Myanmar</b>	WHO network	Yes (quarterly)	Yes
<b>Maldives</b>	No organized surveillance	–	–
<b>Nepal</b>	WHO network	Yes (quarterly)	Yes
<b>Sri Lanka</b>	WHO network	Yes (monthly)	Yes
<b>Thailand</b>	Ministry of Public Health	Yes (annually)	No

IEDCR: Institute of Epidemiology, Disease Control and Research

It was apparent that all the WHO-coordinated sentinel sites were sharing data with respective ministries of health. However, frequency of data sharing was variable and the initiative by the sentinel surveillance sites was informal, without any demand from the ministries of health. Therefore, in order to consider more formal integration through sharing of surveillance information, the group discussed how the respective ministries of health should be approached and the focal person or unit that could be

approached for integrating RVGE surveillance into VPD network. They identified whether the responsible unit is a disease surveillance unit that is separate from the NIP. The outcome of the discussion is summarized in Table 3.

**Table 3. How to approach the ministries of health for integrating RVGE surveillance into VPD surveillance networks**

<b>Country</b>	<b>Ways to approach the ministries of health</b>	<b>Unit in the ministries of health to be approached</b>	<b>Separateness of the unit from the NIP</b>
<b>Bangladesh</b>	Health ministry already aware	IEDCR	Separate
<b>Indonesia</b>	Meeting with health ministry	NIP	Not separate
<b>Maldives</b>	Meeting/communication with health ministry	Disease Surveillance Unit under Centre for Community Health and Disease Control	Separate
<b>Myanmar</b>	Meeting with Central Epidemiology Unit	Central Epidemiology Unit under Disease Control Unit	Not separate
<b>Nepal</b>	Communication with Division of Child Health in Department of Health	NIP under Division of Child Health	Not separate
<b>Sri Lanka</b>	Communication with Deputy Director General (public health services)	Epidemiology Unit of health ministry	Not separate
<b>Thailand</b>	Meeting with Disease Control Unit of the health ministry	Bureau of Epidemiology of Disease Control Unit	Separate

IEDCR: Institute of Epidemiology, Disease Control and Research

Representatives of the RVGE sentinel surveillance networks highlighted the need for facilitating technical and logistic support for the current sentinel surveillance sites by the ministry of health in the event of integration. Regarding the issue of diverting of donor funds directly to the country, as in the case of immunization system strengthening, participants preferred the current system of channelling funds through WHO to the implementing organization. The group members proposed following variables to be included as the core variables in the reporting format of surveillance information to the ministry of health.

- name of the sentinel site
- number of enrolled cases during the quarter
- monthly distribution of enrolled cases
- age distribution of enrolled cases
- number (%) of faecal specimens taken for rotavirus testing
- number (%) of rotavirus positive specimens
- clinical information based on the requirement of the ministry protocol.

### ***IB-VPD surveillance***

The IB-VPD working group agreed that the first step of step-wise mechanism/s for integration of IB-VPD surveillance is sharing surveillance information with the respective ministries of health. Participants also analysed the current status of integration of IB-VPD sentinel surveillance sites into the existing national disease surveillance networks by sharing the data/information generated by sentinel sites in participating countries. The status is summarized in Table 4.

**Table 4. Current status of integration of IB-VPD sentinel surveillance sites into existing VPD surveillance (by sharing of surveillance information)**

<b>Country</b>	<b>Mechanism of integration</b>	<b>Reporting format</b>	<b>Reporting frequency</b>	<b>Year initiated</b>	<b>Impact of evidence-based decisions</b>
<b>Bangladesh</b>	No formal mechanism of data sharing. However, site shares data with policy-makers and health ministry as a part of advocacy.	Published data, brochures, handouts, meetings etc.	Needs-based and occasional	2009	Data sharing is not regular, but health ministry and EPI use data for policy decisions.
<b>India</b>	<ol style="list-style-type: none"> <li>1. Vellore laboratory receives isolates and data from sites.</li> <li>2. Compiled report sent to the NIE, ICMR and health ministry.</li> <li>3. Report discussed quarterly at stakeholders meeting with representation from all sites, National Centre for Disease Control and ICMR (both under health ministry, but run independently).</li> </ol>	Similar to WHO format	Monthly	2011	<p>NIE organizes half yearly meeting with Vellore laboratory, health ministry (immunization division) and all sentinel surveillance sites.</p> <p>However, impact is minimal on policy decisions</p>

Country	Mechanism of integration	Reporting format	Reporting frequency	Year initiated	Impact of evidence-based decisions
<b>Nepal</b>	Report sent to Child Health Division at health ministry	Similar to WHO format	Quarterly	2010	National Committee of Immunization Practices organizes meeting quarterly and invites other parties to discuss issues. Considers surveillance data in decision-making
<b>Sri Lanka</b>	Already integrated. All surveillance data are compiled by Epidemiology Unit of health ministry. Study run by, and data owned by, the Government.	Similar to WHO format	Monthly	2009	Data owned by the Government. Hence, significant impact on policy decisions

NIE: National Institute of Epidemiology

Based on the analysis of the current status of IB-VPD data sharing with the respective ministry of health, the group recommended the following:

- despite informal sharing of surveillance data by sentinel surveillance sites, there should be a formal data sharing mechanism in place;
- a comprehensive IB-VPD surveillance dataset should be shared quarterly in a simpler format that carries an advocacy touch. In addition, sentinel surveillance sites may consider sharing the excel-based WHO reporting format;
- to enhance the impact of surveillance information on evidence-based decision-making, it was suggested to consider an attractive format of policy briefs for advocacy and influencing policy decisions.

### **3. Conclusions and recommendations**

Concluding the intercountry workshop on IB-VPD and RVGE surveillance, the participants made the following recommendations.

- IB-VPD and RVGE sentinel surveillance sites:
  - to formally share surveillance data on a quarterly basis with concerned departments in respective ministries of health;
  - to design innovative advocacy materials to facilitate evidence-based policy decisions related to IB-VPD and RVGE surveillance and ensure mobilization of the support of health ministries, based on individual country-specific needs.
- RVGE sentinel surveillance sites to implement regional SOPs with a view to standardizing RVGE laboratory practice in the Region.
- WHO and the RRL to develop and share regional SOPs (including storage, packaging and transportation of samples) on IB-VPD laboratory practices for implementation, with a view to standardizing laboratory practices on IB-VPD in the Region.
- Enhance national laboratory capacity, improve quality of laboratory data and strengthen quality control systems in sentinel surveillance sites and national laboratories pertinent to IB-VPD and RVGE surveillance.
- WHO headquarters to share the expected list of variables and data dictionary for:
  - collection of case-based data on IB-VPD with the sentinel sites;
  - collection of data from the RRL.
- Principal investigators to inform WHO regarding their willingness to share the expected list of variables with WHO.
- WHO Regional Office for South-East Asia to inform WHO headquarters of the regional position on sharing case-based details.
- Sentinel surveillance sites to continue using the current WHO data reporting formats of aggregated data for IB-VPD and RVGE.
- RRLs to provide feedback to sentinel surveillance sites.

## **Annex 1**

### **Agenda**

- (1) Opening session
- (2) Global update on RGVE and IB-VPD surveillance
- (3) Regional update on RGVE and IB-VPD surveillance
- (4) Discussion on issues and challenges encountered by sentinel surveillance sites
- (5) Global experience of integrating IB-VPD and RVGE into VPD surveillance networks
- (6) Group discussion on establishment of the mechanism for integration of rotavirus and IB-VPD surveillance to the VPD network in the South-East Asia Region
- (7) Global Reference Laboratory update on IB-VPD and expected regional standards
- (8) Global Reference Laboratory update on rotavirus surveillance and expected regional standards
- (9) RRL update on rotavirus surveillance: issues. challenges
- (10) RRL update on IB-VPD surveillance: issues. Challenges
- (11) Discussion on feasibility of implementation of regional SOPs on rotavirus laboratory practices
- (12) Planning for post-introduction impact evaluation of pneumococcal vaccine in Bangladesh
- (13) Standardized data reporting and quality of data: global expectations
- (14) Discussion on measures to improve quality and standardized reporting of surveillance data to ministries of health and WHO

## Annex 2

### List of participants

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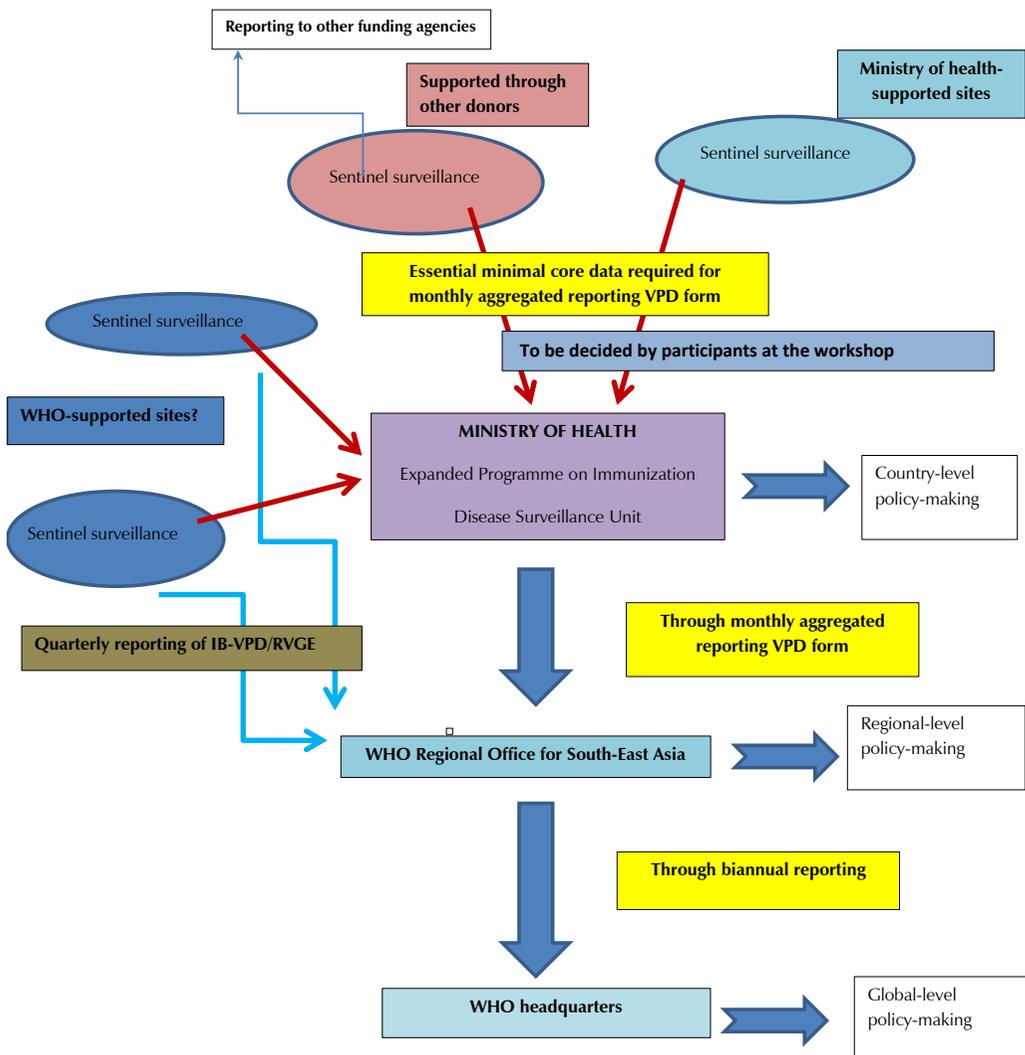
Mr Tika Sedai  
TIP – Data Manager  
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### **Secretariat**

Mr Ravinder Negi  
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### Annex 3

## Conceptual framework for integration of IB-VPD and RVGE surveillance into the existing VPD surveillance networks in Member States



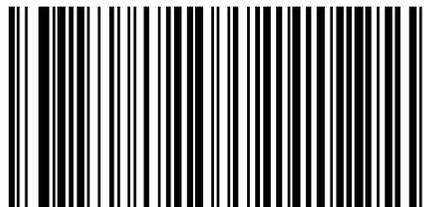
An intercountry workshop on sentinel surveillance of invasive bacterial vaccine-preventable diseases (IB-VPD) and rotavirus gastroenteritis (RVGE) was held from 20 to 21 June 2013, in New Delhi, India. The objective of the consultation was to further strengthen sentinel surveillance of IB-VPD and RVGE with a view to generating evidence on disease burden due to these diseases in the South-East Asia Region. The workshop brought together participants from WHO-coordinated sentinel surveillance sites, other sentinel surveillance networks in Member States, sentinel surveillance site laboratories/national laboratories, regional reference laboratories for IB-VPD and RVGE surveillance, the Regional Office for South-East Asia and WHO headquarters. Participants were provided with updates on the global and regional status of IB-VPD and RVGE surveillance and laboratory networks, as well as global expectations for standardizing laboratory practice and data management. Furthermore, participants agreed upon the initial step of incorporating IB-VPD and RVGE surveillance into existing vaccine-preventable disease surveillance in respective countries. The report includes the proceedings of the technical sessions, outcomes of the group work, and recommendations made by participants to further strengthen sentinel surveillance of RVGE and IB-VPD in the WHO South-East Asia Region.



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