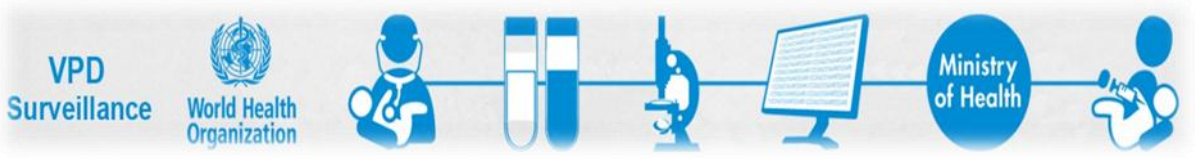

EXECUTIVE SUMMARY
2013 GLOBAL STRATEGIC REVIEW OF THE INVASIVE BACTERIAL VACCINE PREVENTABLE DISEASES AND ROTAVIRUS SURVEILLANCE NETWORKS

Genesis of the strategic review

Since 2008, WHO has been coordinating global sentinel hospital surveillance networks for invasive bacterial vaccine preventable diseases (IB-VPD) and rotavirus (RV) to provide quality data to assist with planning of public health programs around vaccine introduction and use. The objectives set for the network in 2008 were:

- During the pre-vaccine introduction period:
  - Document presence of disease, describe the disease epidemiology and provide data for estimating disease burden;
  - Establish a system to measure impact after vaccine introduction;
  - Identify circulating serotypes and measure serotype distribution; and
  - Monitor antibiotic sensitivity.
- During the post-vaccine introduction period also:
  - Assess disease trends over time;
  - Monitor vaccination program impact;
  - Monitor changes in circulating strains/serotypes; and
  - Develop a platform for effectiveness and safety evaluation.

The longer term vision has been to establish sentinel surveillance for selected vaccine preventable disease (VPD) in low- and middle-income countries to complement existing active surveillance for polio, measles/rubella and passive surveillance and reporting for other VPDs.

In February 2013, following 5 years of network coordination, WHO launched a full strategic review of both networks with its informal Technical Advisory Group for new vaccines surveillance (iTAG) to identify the networks' strengths and weaknesses and to prioritize future actions. The iTAG assessed the networks capacities to document vaccine impact via the accelerating introductions of pneumococcal conjugate and rotavirus vaccines in the light of the call for quality case-based surveillance in the 2011-2020 Global Vaccine Action Plan. Recognizing the resource constraints in the targeted countries and competing health priorities, it was deemed imperative to determine best strategies to target human and financial resources.

At the review's outset, the iTAG and WHO recognized that while great strides had been made in the development of both IB-VPD and RV global surveillance networks, improvements were still required to ensure strong and effective networks that meet the ultimate goal of providing reliable data. IB-VPD surveillance was particularly recognized to be more complex than RV surveillance due to lack of adequate methods for laboratory confirmation of pneumococcal pneumonia, the rarity of meningitis as compared with diarrhoea, the difficulties of specimen collection and transport, and the complex bacterial laboratory diagnostic testing required.

Prior to this review, in November 2012, WHO had established the following criteria for IB-VPD surveillance, in order to prioritize sites for support:

- Presence of a country surveillance management team, consisting of focal points at Ministry of Health (MoH), sentinel hospital, sentinel hospital laboratory, and for data management;

- Countries conducting only Tier 1 meningitis surveillance enrol at least 100 suspect meningitis cases[1] in children <5 years of age[2];
- Data is reported regularly to WHO according to the schedule agreed with the WHO Regional Office; and
- The hospital sentinel sites participate in the WHO IB-VPD laboratory external quality assessment programme.

Objectives and methodology of the 2013 strategic review

The strategic review was conducted under the oversight of the iTAG that has been advising WHO on the conduct of sentinel surveillance since July 2011. The iTAG and WHO agreed on the following objectives for the strategic review:

1. Assess whether and to what extent the original 2008 objectives for the networks were met.
2. Critically assess the Ministry of Health (MoH) perspective, laboratory networks, and WHO activities for capacity building, funding, and data management and the use of data; and
3. Provide conclusions and recommendations for strengthening the networks including defining any needed complementary approaches for IB-VPD surveillance, and critically assess the networks' future utility as a platform for other vaccine preventable disease (VPD) surveillance.

The strategic review consisted of several methods including analysis of surveillance data; questionnaires to obtain MoH perspectives; external review of laboratory function; external review of data management; review of the literature and GAVI applications to evaluate whether WHO surveillance data has been used in decision making; internal review of WHO activities and funding disbursement.

Analysis of surveillance data was conducted on all data available to WHO, including IB-VPD case-based data collected by 4 Regional Offices (ROs) and data aggregated by sentinel site in 2 ROs. For RV, data for analysis was aggregated by sentinel site. Data from over 90 databases were consolidated and cleaned. IB-VPD variables were mapped across Regions, and the first uniform IB-VPD data analysis performed. Due to the volume of data and paucity of time, the iTAG and WHO agreed that sites would be categorized and analysis focused on sites that met defined performance characteristics to determine whether they achieved the original 2008 objectives.

For IB-VPD, sites that reported data during 2010 to 2012 were categorized as:
- New sites: site began reporting in 2011 or 2012
- A Sites: met both of the following criteria
    - Reported data in ≥11 months per year for at least two years during 2010-2012.
    - Enrolled ≥100 suspected meningitis cases per year for at least two years during 2010-2012 (tier 1) or enrolled ≥500 suspected meningitis/pneumonia/sepsis cases per year for at least two years during 2010-2012 (tier 2).
- B Sites: met both of the following criteria
    - Reported data in ≥10 months per year for at least two years during 2010-2012.
    - Enrolled a total of ≥100 suspected meningitis during 2010-2012 (tier 1) or enrolled ≥500 suspected meningitis/pneumonia/sepsis cases during 2010-2012 (tier 2).
- C Sites: Sites that improved in consistency of reporting and case enrolment between 2011 and 2012 but did not meet the criteria of A or B sites.
- D Sites: All other sites.

[1] Any child aged 0-59 months admitted to a sentinel hospital conducting surveillance with sudden onset of fever (> 38.5 °C rectal or 38.0 °C axillary) and one of the following signs: neck stiffness, altered consciousness with no other alternative diagnosis, or other meningeal sign OR very patient aged under 5 years of age hospitalized with a clinical diagnosis of meningitis.

[2] Countries that do not enroll 100 suspect meningitis cases during 2013 but that significantly increased the number of enrolled cases over 2012 will be considered for funding on a case-by-case basis.

For RV, analysis focused on sites that reported ≥ 10 months of data during 2011 and 2012 as well as enrolled ≥ 100 cases during those years.

The iTAG and WHO collaborated closely during the strategic review via monthly conference calls to agree on the scope of the review and data analysis plan, as well as to assess progress made, and review data that had been collated. Additional ad hoc technical discussions focused on IB-VPD or RV specific issues and data. The results of all methods were reviewed at a 5 day meeting beginning the week of the 16th of September 2013, which brought together the iTAG, WHO and its partners to formulate agreed conclusions and recommendations.

Key findings of the 2013 strategic review of the IB-VPD and RV surveillance networks

1. IB-VPD surveillance findings

In 2008, the IB-VPD network comprised 36 reporting countries (69% GAVI-eligible) with 91 sites (60% in GAVI countries) that enrolled 16,124 children with meningitis and 20,098 children pneumonia /sepsis. In 2012 the network comprised 58 reporting countries (79% GAVI-eligible) with 150 sites (70% in GAVI countries) that enrolled 20,098 children with meningitis and 35,480 children with pneumonia and sepsis. Sites[1] that received financial support (e.g. sites in GAVI-eligible countries), in general, performed better. Excluding the 37 new sites, 48 (52%) of the 93 GAVI sites conducting meningitis surveillance were categorized as A, B, or C sites while only 10 (20%) of the 51 non-GAVI sites were (Table). Among the 34 category A sites conducting meningitis surveillance, 32 (94%) were located in GAVI-eligible countries.

Table: Invasive bacterial vaccine preventable disease surveillance sites conducting meningitis surveillance by category based on data reported to WHO, 2010 to 2012.

Sites Conducting Meningitis Surveillance	**Category of Site**				
	A # (%)	**B** # (%)	**C** # (%)	**D** # (%)	**Total** # (%)
GAVI sites	32 (94)	14 (64)	2 (100)	45 (52)	93 (65)
Non-GAVI sites	2 (6)	8 (36)	0	41 (48)	51 (35)
Total	34 (100)	22 (100)	2 (100)	86 (100)	144 (100)

*The 37 new meningitis sites are excluded; 28 of these sites are in GAVI-eligible countries.

The strategic review team agreed that the current IB-VPD network had met the original 2008 objectives for documenting presence of disease (e.g. 61 of 65 countries that reported data during 2008 to 2012 documented presence of pneumococcus), using surveillance as a platform to conduct special studies (e.g. Brazil and Mongolia), and using data to inform vaccine introduction decisions. Capacity for conducting surveillance had been built, not only for meningitis but for other VPDs (such as typhoid detection). Some countries had 2 years baseline data of pneumococcal isolates and 1 year post-PCV introduction data. However, the laboratory network assessment (see Annex) suggested that countries, regions and HQ were not working together as a network. The data generated was not being used in the most efficient and effective manner (see Annex). Because of the need for high-quality data and resource constraints, it was concluded that the investment of financial and technical support should be focused upon a smaller number of sites.

2. RV surveillance findings

During 2008-2012, 265 sites in 67 countries reported any data to WHO. Among sites that reported data during 2011-2012, 79 sites (80% GAVI-eligible) in 37 countries (86% GAVI-eligible) met the inclusion criteria. Thirteen of the 37 countries had introduced RV vaccine nationally, and 1 country introduced sub-nationally. Most sites included in the analysis met the

[1] Year-to-year variability in the number of reporting countries and sites exists due to reasons including in-country conflict, and political change.

targets for the 6 established surveillance performance indicators. Among these sites, the mean RV detection of the 75,353 tested children was 36%, with the largest percentage positive (42%) in the 6-11 month age group. Sixty-five deaths among RV positive cases were reported, with the case fatality ratio ranging from 0% to 5.9% of cases by site. RV seasonality differed by region and by AFR sub-region, with seasonal peaks seen more obviously in AMR, EUR, WPR and the AFR south sub-Region. Guatemala had sites that met the inclusion criteria and had at least 2 years pre- and two years-post RV vaccine introduction data. In Guatemala, the proportion (mean) of children hospitalized with diarrhoea with RV dropped from 42% in the 2 years pre-vaccine introduction was 42% to 28% in the second year post introduction.

The strategic review team agreed that the RV network met the original 2008 objectives for documenting presence of disease, describing disease epidemiology, using surveillance as a platform for special studies in some countries, and using the data for policy decisions. At least 37 (55%) of 67 participating countries had collected at least 2 years of pre-vaccine introduction data that met the inclusion criteria for quality as defined via the strategic review.

3. Assessment of IB-VPD and RV laboratory networks

The independent assessment of the laboratory networks found both laboratory networks had made '…*huge advances in strengthening national and regional laboratory capacities, standardization of laboratory testing, improving laboratory quality and performance, and establishing functional international networks. Both, however, remain in a state of development. Of the 2 laboratory networks, the RV network is significantly closer to achieving effective support of the programme. The RV laboratory network has inherent advantages over the IB-VPD laboratory network in that not only is laboratory testing significantly less complex, but laboratory requirements are more compatible with those of existing global networks, including polio and measles/rubella. … While WHO has been very effective in providing and contributing to technical guidance of the laboratory networks, provision of overall management and oversight has been less impressive. …The fidelity with which laboratory data is entered into the reporting system and the completeness of reporting is clearly inadequate. This problem can be addressed to some extent by ensuring strict linkage between laboratory data and clinical and epidemiology data through the more effective use of unique case ID numbers. This is not a technical problem; it is one of network management and oversight.*' (full report in Annex).

4. MoH perspectives

Standardized questionnaires were received from 27 MoH respondents in AFR, 13 in EMR, and 8 from WPR. Respondents noted the main reasons for establishing surveillance were to assess disease burden, prepare for vaccine introduction, monitor vaccine impact, and to strengthen bacterial laboratory capacity. Overall, 89% of respondents felt surveillance provided information to advocate to, or within, the government on the importance of rotavirus diarrhoea or paediatric bacterial meningitis. National surveillance was reported as the most important factor in the decision to introduce a vaccine or to continue national funding for a vaccine, followed by availability of other national data (e.g. special studies, passive national health systems) and disease burden estimates from WHO or the literature. MoH respondents noted a desire to increase the number of existing sentinel sites in order to obtain more representative data for their country.

5. WHO support to the network

To achieve the aim of good quality data, WHO recognized the necessity of a solid infrastructure for surveillance; thus, WHO's activities during the past 5 years have been to develop the building blocks such as instituting laboratory external quality assurance, standardized sentinel site assessments, and training. In addition, WHO provided sites with specimen collection and laboratory supplies including rapid diagnostic kits. Access to advanced laboratory testing was provided via molecular testing at reference laboratories. Regional and global meetings brought together network members to share experiences and foster the feeling of belonging to a

network, supported by the dissemination of twice yearly global surveillance bulletins. To improve quality, IB-VPD communication tools (posters and pamphlets) to support specimen collection, identifying bacterial causes of meningitis, and data management were also developed and distributed to sites. A field-based method for estimating the denominator of at-risk children at a sentinel hospital was developed for meningitis surveillance to better understand catchment populations and enable estimation of incidence of meningitis hospitalizations.

From 2008 to 2012, GAVI provided $45.5 million in support of both surveillance networks of which $8.8 million (19%) supported WHO staff and $36.7 million (81%) supported surveillance activities. In general, two-thirds of activity funds supported the surveillance infrastructure of the reference laboratory network, regional/global meetings, trainings, technical support, and one-third supported sentinel sites including purchase of supplies. Additional funding provided by the U.S. Centers for Disease Control and Prevention included $530,000 for standardized site assessments, middle income countries and the data landscape analysis, as well as provision of 3 full-time staff and additional technical support.

The current year-to-year funding with uncertainty around funding sustainability has caused hesitation by countries and WHO to implement improvements. This uncertainty has been a particular problem for reference laboratories as the year-to-year funding prohibits hiring of staff and long-term planning. This has led to one reference laboratory withdrawing from the network.

6. Data landscape analysis findings

The assessment found the '*data management process is variable by WHO RO, and the data transfer and reconciliation process is cumbersome and time-consuming. Thus, it is warranted to explore new and different options to streamline the current system, while taking into account the unique setting and needs of each WHO RO. The general data flow in each RO is consistent … Data capture occurs at a sentinel site, sent to the country office, and then sent to the regional office and then finally submitted to HQ. Two of the ROs have opted to only collect aggregate data while the other 4 collect case-based data…Every RO has implemented a standard paper case report form, however … Each country and even site…may have made modifications to the standard forms to allow for capture of other variables... Every RO has implemented some type of standard data collection tool, however there is not any standardization across the tools. Some of the major factors affecting the quality of data …include relationship with Regional Reference Labs* [RRL] *with inability to link RRL data* [to the individual case data] *due to lack of use of unique identifiers and the general availability of resources and funding. A future data management system …needs to be flexible and dynamic to account for the different data infrastructures and approaches of each RO. The goal of the new system would to provide a centralized system which would allow for decentralized management and control of data in a case-based format'* (full report in Annex)

Key conclusions and recommendations from the 2013 strategic review

1. IB-VPD surveillance: Conclusions and recommendations

The IB-VPD programme is at a critical juncture in its development, and decisive changes will be necessary to produce high-quality data. It was recognized that building a strong and effective IB-VPD surveillance network is both complex and challenging. The overall opinion amongst all partners involved was a strong desire to continue strengthening the network; however, it was agreed that the quality of the network must be urgently improved, and that both technical and financial support should be targeted to a smaller number of sites. In the short-term, these sites would be those that met the defined funding criteria and minimum standards (in general, the A, B, and C category as well as new sites joining the network since 2011). The strategic review team recognized that the category D sites, in general, required investment of considerable human and financial resources before capacity is generated to produce quality data; thus, exclusion of Category D sites would enable focus on the other sites to further improve quality.

Furthermore, it was discussed and agreed by ROs, HQ, and partners that collection and sharing of case-based data across all levels is essential to conduct the necessary data analysis to monitor and evaluate the programme, as well as to link clinical and laboratory data particularly of serotype/group data. Data analysis should be conducted more frequently and actively used to monitor surveillance performance and outcome. Strengthening serotype/serogroup data availability and usefulness is also of importance.

Recommendations for the IB-VPD Network Size and Scope

- Network participation requires meeting minimum data quality standards regarding consistent reporting, enrolment of cases, laboratory, and surveillance performance indicators. In principle, all (GAVI and non-GAVI eligible) countries should be encouraged to participate in the network; however, network size may need to be limited as WHO support to countries to ensure generation of high-quality data is subject to financial and human resource constraints;
- In the coming year, the current number of sites in each country should not be expanded unless there is a compelling reason to do so. Since MoH expressed a desire to expand the number of sites, WHO should engage MoH officials in further discussion around this issue;
- Only sites that meet the established funding criteria should receive funding in 2014. Sites categorized as D, in general, do not meet these funding criteria, and should not be provided with GAVI funds, if located in GAVI-eligible countries. This decision should be based on data provided during the first 6 to 9 months of 2013, and countries should be notified of the decision by February 2014 (which is prior to receipt of 2014 funding);
- During early 2014, additional work is required to clearly define longer-term network objectives, as well as performance and funding criteria. Detection of a minimum number of pneumococcal cases per site per year in countries which have not introduced PCV should be included as a metric. Additionally, sites should be further categorized as:
    - 'Fully recognized site': site has been assessed within the past 2 years using the WHO standardized assessment tool, and is providing quality data for measuring vaccine impact (in pre-PCV introduction countries) or for monitoring serotype epidemiology (post-PCV introduction countries);
    - 'Supported site" site receives funding from WHO, agrees to share case-based data on a quarterly basis, and is either a fully recognized site or working towards that;
- Networking should be strengthened to share resources and to enhance laboratory collaboration with measles/polio surveillance efforts.

Recommendations for Data Management and Dissemination

- Institute a common case-based data system that shares standardized data across sites/regions/reference labs/HQ, with real-time verification and analysis capacity, and with improved data quality;
- Strengthen data management capacity for data analysis, interpretation and dissemination at all levels; and
- Modify the WHO Global Bulletin to show all reporting countries but limit analysis to a subset of sites reporting quality data, including reporting for at least 12 months and enrolling a minimal number of cases.

Recommendations for the IB-VPD laboratory network:

- Conduct in-depth Regional reviews of laboratory networks function and output to identify region-specific issues and provide region-appropriate priority activities;
- Reduce the number of participating network laboratories to more closely match programme capacity to fully support and supervise these laboratories to an extent that guarantees confidence in reported laboratory results;
- Review and revise the roles and responsibilities of WHO Regional and Global laboratory coordinators to place more emphasis on active management of network performance;
- Every effort should be made to assess every laboratory at least once each year;
- Continue the external quality assurance, and ensure quality control (all positive specimens and 10% sample of negative specimens should be submitted in a 'blinded' fashion for RRL

testing) with data analysis to validate test and laboratory performance;
- Report serotype/serogroup data at least twice yearly to WHO HQ and more frequently to ROs to enable more prompt detection of problems with subsequently actions to improve quality;
- Standardize sample selection for serotyping/grouping; and
- Link case-based clinical and epidemiological data from sentinel sites to local laboratory results and polymerase chain reaction results as well as serotype/group data from RRLs, which may require modification of existing data management systems.

Recommendations for sentinel sites
- Ensure sites meet a definition of a sentinel site so surveillance objectives can be met;
- Initiate zero reporting to enable differentiation between no cases enrolled or no report submitted to WHO;
- Develop strategies to improve performances at all sites (GAVI and non-GAVI) based on findings from monitoring and evaluation of the surveillance system; and
- Prioritize site assessments using external reviewers, MoH, local institutions, etc.

2. RV Surveillance: Conclusions and recommendations

The review team concluded that the RV surveillance network was overall generating quality data useful for decision makers. However, further targeted enhancements to the network would enhance its capacity to provide more standardized information to national, regional, and global policy makers. In particular, all sentinel sites must meet the standard definition for a site so that calculations of rotavirus positivity are based on hospitalized children, rather than children seen at peripheral clinics. Additionally, genotyping data generation should be further strengthened by development of standardized protocols for specimen selection and linking of case-based data that includes clinical and vaccination data.

Recommendations for the overall RV surveillance system
- Network participation requires meeting minimum data quality standards regarding consistent reporting, enrolment of cases, laboratory, and surveillance performance indicators. In principle, all (GAVI and non-GAVI eligible) countries should be encouraged to participate in the network; however, network size may need to be limited as WHO support to countries to ensure generation of high-quality data is subject to financial and human resource constraints;
- The current surveillance performance indicators should be examined for usefulness; and
- Encourage further networking including laboratory collaboration with measles, polio, IB-VPD surveillance and sharing of resources.

Recommendations for Data Management and Dissemination
- Countries should report case-based data to all regional offices and HQ, and gathered data should be further standardized;
- RRLs should report genotype data to ROs twice yearly to ROs, as feasible within current resource constraints; and
- Global Bulletins should be modified to show all reporting countries on a map, but limit analysis to subset of reporting sites that report every month and enrol $\geq$ 100 cases annually.

Recommendations for the RV laboratory network
- Standardize sample selection for genotyping;
- Begin to establish the linkage of case-based data to genotype data;
- Examine country-level genotype distribution in addition to distribution at regional and global levels;
- Build additional technical capacity at the national laboratory (NL) level, if possible; and
- Funding permitting, include all sites in the EQA programme.

Recommendations for sentinel sites

- Ensure sites meet a definition of a sentinel site so surveillance objectives can be met;
- Update eligibility criteria for inclusion in data analyses to include 12 months reporting and ≥100 specimens at a single site (no satellite sites)
- Initiate zero reporting to enable differentiation between no cases enrolled or no report submitted to WHO; and
- Develop strategies to improve performances at all sites (GAVI and non-GAVI). Strategies may be based on findings from monitoring and evaluation of the surveillance system.

3. IB-VPD and RV future vision and complementary approaches for IB-VPD surveillance: Conclusions and recommendations

Recommendations for complementary approaches to IB-VPD surveillance

For IB-VPD, there is an urgent need to improve the quality of the data, and to monitor ongoing serotype epidemiology. However, it is anticipated that data quality will be unable to quickly reach the desired level in all countries, particularly those with the weakest health and hospital systems. Thus, a complementary strategy to IB-VPD surveillance for measuring vaccine impact is required.

- Develop tools and processes (models) that allow PCV impact assessment by input of quality data from IB-VPD as well as complementary existing data sources including pneumonia morbidity and mortality.

Recommendations for assessing future utility for surveillance of other VPDs

Both the IB-VPD and RV sentinel hospital surveillance networks have developed a surveillance platform of improved epidemiological and laboratory capacity. Careful consideration is warranted to determine whether other VPD surveillance activities can be added to this platform, without jeopardizing the quality of IB-VPD and RV data.

- Define how to best build upon these networks to conduct surveillance for other VPDs, including those prevented by current vaccines and future vaccines such as typhoid, as well to increase capacity for outbreak detection.
- Appropriate surveillance approach(es) for other VPD's should be developed based on the specific disease characteristics (incidence, hospitalization, diagnostic testing characteristics, etc.) and the key objectives for surveillance of that disease.

Recommendations for monitoring implementation of the strategic review's recommendations

- The iTAG should continue to engage in the on-going progress made from implementation of these recommendations via quarterly teleconferences or meetings, and advice WHO on any corrective actions that may be required.

Recommendations for funding

- Improvement of the data management system with a move to case-based data (including linking of data from reference laboratories) and more on-going data analysis, interpretation and dissemination will require additional financial support. Longer term funding would enhance commitment to make changes in the system.