Report of the Global New Vaccines Surveillance Meeting for Rotavirus and Invasive Bacterial Vaccine Preventable Diseases, September 2011

And

Prioritized Activities to Advance Both Networks during 2012

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I. EXECUTIVE SUMMARY.

Background:
Both the invasive bacterial vaccine preventable diseases (IB-VPD) and rotavirus surveillance networks have made, and continue to make, significant progress over the past years. A major accomplishment has been the transition of independent IB-VPD and rotavirus surveillance sites and networks into one WHO global coordinated surveillance network during 2008 and 2009. As a consequence, twice annual surveillance bulletins are now distributed globally, using data provided by Ministries of Health (MoH) to WHO using standardized processes. Global, regional and national laboratories have been identified and are working to support sentinel hospital site laboratories in order to continue development of the surveillance networks. Data management processes are being standardized to provide a uniform global approach to new vaccine surveillance with adherence to standardized procedures and case definitions.

Objectives of the 2011 Global New Vaccines Surveillance Meeting:
1) Review and discuss progress made in implementing recommendations from the 2010 global surveillance meeting;
2) Review in detail data generated by both surveillance networks; and
3) Agree on prioritized steps to advance both networks over the next 12 months.

Meeting Structure:
Representatives from the WHO HQ, Regional Offices, MoH, Global and Regional Laboratories and invited immunization experts, met in Geneva in September 2011 to discuss the meeting objectives. The meeting included a closed session for WHO internal discussions and then was organized into plenary areas that targeted the two laboratory networks, data management, use of surveillance data for national decision making and enhancing the role of the MoH via monitoring and supportive supervision activities. During the final session, participants received feedback on the findings and recommendations with agreed milestones and timelines for the next 12 months.

Findings:
Of the 46 recommendations made from the 2010 global surveillance meeting, 39% were completed with 48% either partially met or in progress. The launch of the laboratory external quality assessment (EQA) programmes for both networks during 2011 was viewed as a critical step to target efforts to further improve data quality.

IB-VPD Tier 1: meningitis surveillance (CSF specimens): During 2010, data varied considerably among the 48 reporting Member States with a range from 4% to 98% of probable bacterial meningitis cases detected among suspect cases, and 7 (15%) countries not detecting any vaccine preventable disease (VPD) organisms. Despite substantial gains in developing the IB-VPD network over the past 2 years, it was agreed that Tier 1 remains the weakest area within the overall new vaccines surveillance networks. During the coming months, an assertive effort to improve Tier 1 surveillance was noted to be of paramount importance. A much stronger, cohesive and coordinated infrastructure for the network is needed, not only to maintain the gains made but, as importantly, to support future growth and development. To that end a Tier 1 Surveillance Matrix was developed to give clear vision and direction that includes among other activities, on site assessments,
development of case-based reporting, standardization of laboratory processes, and the necessity for all sentinel sites and laboratories to meet an agreed pre-requisite criteria within a 12 month period in order to receive continued financial support. This will also apply to future sites joining the network.

**IB-VPD Tier 2: pneumonia-sepsis-meningitis surveillance (blood and CSF specimens)** Sixteen countries reported data during 2010, with blood cultures obtained from 15,454 (55%) of the children with suspected pneumonia cases and 1.3% of the cultures positive for a VPD. Tier 2 was noted to continue signs of sustained development and the production of credible data with countries beginning to use output data for policy making decisions.

**Rotavirus.** During 2010, 61 countries reported surveillance data, with 40% of children hospitalized with diarrhoea found to have rotavirus infection. It was agreed that this network continues to operate a robust system with an increasing number of countries providing quality data which is being used for governmental decision policy making.

**Conclusions:**
The WHO coordinated global surveillance for both networks has continued to develop and expand over the past 12 months. Both rotavirus and IB-VPD Tier 2 surveillance networks were found, overall, to be producing reliable data. However, considerable improvement is still required specifically with regards to the IB-VPD Tier 1 network. Thus, the main meeting conclusions were:

- **Focus on IB-VPD Tier 1:** The focus of activities for the next 12 months should clearly be channelled into Tier 1 to improve data quality and secure greater ownership and an enhanced role of the MoH.

- **Further develop the bacterial laboratory network particularly for Tier 1:** The global EQA programme should be fully utilized to best target laboratories still requiring further support; rapid diagnostic testing should be available at sentinel hospitals to ensure decreased diagnostic variability; National (NL) and Regional Reference Laboratory (RRL) expertise should be used to provide molecular testing (i.e. polymerase chain reaction [PCR]) support for sentinel hospital sites via shipment of specimens to the reference laboratories for testing. Global laboratory guidelines and standard operating procedures would encourage standardization of laboratory processes.

- **Increase regular monitoring and supportive supervision assessments to rotavirus and IB-VPD sentinel sites with provision of specific recommendations to improve practices.**

- **Improve data management for IB-VPD surveillance by seeking to develop a case-based reporting strategy and a methodology to identify rapidly a population denominator for sentinel sites.**

- **Secured funding remains a critical factor to the future network both in terms of ongoing daily operations and in ensuring the implementation of the meeting recommendations to ensure the future development of the networks.**
II. MEETING CONCLUSIONS AND RECOMMENDATIONS: PRIORITIZED ACTIVITIES TO ADVANCE BOTH NETWORKS DURING 2012

II a. WHO closed session.
WHO regional office (RO) and headquarters (HQ) staff met to review the status of the surveillance networks and agree on key activities to improve the network.

The following agreements were reached: (see relevant sections of the full report for more details)

• **IB-VPD funding criteria should be established**: In order to set a minimum standard of quality for the IB-VPD network, WHO will develop a minimum set of eligibility criteria that countries will need to meet in order to obtain IB-VPD surveillance funding.

• **WHO staffing in some offices needs to be expanded**: The lack of WHO staff in some specific offices hampers the work to improve the surveillance network. WHO will work to fill these positions.

• **Data management processes will be standardized and strengthened**:
  - The IB-VPD surveillance will be transitioned to case-based reporting, based on adequate WHO staffing and agreements on data safeguarding.
  - VPD organisms detected in suspect meningitis cases, in addition to probable bacterial meningitis cases, will be reported.
  - The current data management collection process will only be revised at a maximum once every two years following joint discussion by the ROs and HQ during the surveillance meeting.
  - Case definitions were reviewed and agreed for rotavirus, and meningitis (suspect, probable, confirmed). (See page 13 for the agreed definitions.)

• **Laboratory: EQA will be continued; global QC will not be started; IB-VPD sentinel laboratory assessment tool will be shortened and protocols developed for RV genotyping**:  
  - The planned global laboratory QC programme will not be launched, as it might be duplicative with the Regional QC programmes monitored by the RRLs.
    - The privacy of the countries during these processes should be maintained to the degree feasible.
  - The IB-VPD sentinel site laboratory assessment tool should be shortened and reorganized. The current tool is appropriate for assessing RRLs pending slight modifications.
  - Clearer protocols are required to guide which RV specimens are sent for genotyping.

II b. Data Management.
AFR, AMR, EMR and WPR presented their data management system. All four regions developed a database system to use at country and regional levels. The data collection is monthly in AFR and EMR while it is quarterly in WPR. AMR has an online data collection system with continuous possibility for update. All regions reported that data is analysed frequently and widely used. The major weaknesses
identified in most regions are the weak data management structure at the country level and problems in the quality of the data reported.

**Priority actions** were identified in order to improve the quality of the data reported and strengthen the data management platform:

- **Minimize revision of variables and data collection template.** When revision is necessary, revise the variables during a consensus meeting and allow enough time to implement changes. The minimum period between revisions should be 2 years.
  - The current template and list of variables will be revised after the surveillance meeting to include the reporting of the VPDs in suspected meningitis cases (Spn, Hi, NM) as well as probable bacterial meningitis cases.
  - This above template and the existing RV template will be used for the next 2 years.

- **Reporting deadlines and timelines from ROs to HQ will be modified as follows:**
  - The current reporting periods will be maintained (May and November.) However, data reported in November will include the previous year’s data and the first 6 months of the current year.
  - **Data reporting: time periods and frequency from RO to HQ:**
    - 1) May: January to December data of the previous year
    - 2) November: January to June of the current year and the previous year’s data.
  - Firm deadlines will be set up for the data that will be included in the bulletins. Data received after the deadline will not be included in the bulletin.

- **In preparation of case based data collection,** WHO HQ needs to obtain an agreement from all partners and to provide regions with:
  - A statement on how the data will be used.
  - A list of variables and a data exchange format.

Additionally, the transition to case-based IB-VPD surveillance reporting is pending on adequate WHO staffing to develop the required technical infrastructure.

- **Additional staff are needed, especially:**
  - For data management functions at the sentinel site.
  - Data management functions at the national level.

- **Data quality should be improved by:**
  - Promoting regular data review meetings with national MoH and sentinel sites, involving surveillance and laboratory coordinators and data managers.
  - Regular training of data managers at sentinel sites/national levels that include points beyond data management, such as basic issues regarding surveillance.

- **Improved communication** on how the data is used in order to improve the motivation at the sentinel site
  - Consider translating the global bulletin into other languages (Spanish, French, etc.)

- **Continued and enhanced collaboration between regional offices and HQ should be undertaken,** and should include a parallel session on data management at the next global surveillance meeting.
II c. Rotavirus Surveillance:  
**MoH management, clinical and other aspects.**

Paraguay, the Sudan, and South Africa summarized their experience in establishing and using sentinel surveillance to guide vaccine introduction decisions. The countries noted that important components of maintaining a strong surveillance system included MoH regular oversight, committed human resources, clear SOPs, and active surveillance centres. The WHO Region of the Americas expanded upon these remarks and agreed with the MoH presenters that RV sentinel surveillance provided data to decision makers around vaccine introduction, improved laboratory capacity, and was valued by MoH. Additionally, the importance of RV surveillance data contributing to the efforts around optimizing vaccination schedules was emphasized.

The following recommendations were made:
1. Support MoH oversight and guidance of sentinel surveillance activities
2. Document the experiences shared in the session so that other countries could benefit from these lessons learned

**Rotavirus Laboratory Network:**

The status of rotavirus surveillance was reviewed in detail for each WHO Region. The rotavirus surveillance network was found to be producing reliable data that could be used by the countries for decision making. RRLs were functioning in each WHO Region, and supporting the network. The global EQA programme was launched in 2011 and was contributing important information to further improve the quality of the network. Similarly, the regional QC programmes were found to be valuable. Genotype distribution in the 6 WHO regions from 2010 surveillance data were presented and differences were identified in the classification of common/uncommon genotypes as well as untypeable genotypes.

The following recommendations were made:
1) Further standardization is required to:
   a) determine which genotypes are truly 'uncommon' and which are 'untypeable';
   b) ensure the agreed global case definition is being used¹; and
   c) clearly define roles and responsibilities of all the partners.
2) Document lessons learned, particularly for AMR, so that countries introducing vaccine in other regions can benefit.
3) More genotype data is needed as vaccine is being introduced globally.
4) Critical laboratory supplies should be assured.
5) On site visits and assessments should be conducted, with recommendations provided to improve the quality of work.
6) Ministries and WHO should integrate RV and IB-VPD surveillance to the degree possible.
7) Continue the global EQA and regional QC systems in order to monitor performance.
   a) A simpler process would be advantageous, such as lyophilization and hand carrying of proficiency testing panels/specimens;

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¹ Rotavirus: Suspect Case: Any child aged 0-59 months admitted for treatment of acute (i.e. ≤14 days) watery gastroenteritis/diarrhoea to a sentinel hospital conducting surveillance. Excluded are children with bloody diarrhoea and children transferred from another hospital.

Conclusions and Recommendations: 2011 Global New Vaccines Surveillance Meeting
b) A standardized follow up corrective action plan is needed for laboratories that do not pass the EQA.
c) A global QC programme is not seen as needed and should not be launched at this stage as there is the global EQA and regional QC programmes that are ongoing.
d) Regional QC programmes should be standardized, in terms of sample size, or percent of positive/negative samples to be QCed at the RRL. SOPs on specimen collection, transport, storage and referral from SS to NLs to RRLs should be developed.
e) A follow up plan should be developed in coordination with the ROs for laboratories that fail the global EQA / regional QC.

8) Focus in consolidating the network, rather than expanding it.
9) Create a small working group of laboratory experts within the network for in depth discussions and to help direct the laboratory network.

II d. Invasive bacterial vaccine preventable diseases (IB-VPD): improving quality of Tier 1 meningitis surveillance

The status of the IB-VPD surveillance network was reviewed in detail for each WHO Region and also from the global perspective. The quality of IB-VPD data must be improved. The following recommendations were made:

- **Ministry of Health ownership** is very important but must be strengthened.
- **Leverage existing surveillance systems; involving NITAGS (National Immunization Technical Advisory Groups) may help improve surveillance and generate advocacy.**
- **Advocacy** should be generated for this network and surveillance in order to ensure decision makers at all levels avail themselves of the data.
- **Reduce the number of participating and supported sentinel sites for IB-VPD surveillance in order to improve the overall quality of data in the remaining sites.**
- **Clearly state the purpose and intent of the surveillance** to ensure partners at all levels understand why the surveillance is conducted, why the data is collected, how this data will be used. Currently, some countries do not fully understand the use of, need for, and value of the resulting surveillance data.;
- **Under the guidance of WHO ROs and WHO laboratory coordinators, RRLs need to take a more proactive role in site visits, improving data quality and assisting ROs in the monitoring of sentinel sites activities.**

**Invasive bacterial vaccine preventable diseases (IB-VPD): Ministry of Health management, clinical and other aspects**

Ministry of Health colleagues summarized their thoughts on how to obtain a high-quality national IB-VPD surveillance system, and made the following recommendations:

- **Supportive supervision, training, and problem solving as needs arise** are key to ensuring high-quality surveillance.
- **Continue sentinel site assessments and site visits.** The capacity of microbiology laboratory staff should be regularly assessed and trainings held as needed.
- **Share the data regularly** within the country and with other Ministries in order to increase awareness of the system generally.
• Conduct quarterly meetings with sentinel sites to problem solve as well as sensitize clinicians, and
• Partnerships between MoH, academic centers (which often collect the best data but often do not submit data to WHO), and others such as the CDC Global Disease Detection colleagues are important to ensure high quality data, but these partnerships can be challenging. An initial step may be in combined efforts to monitor and assess sentinel sites, within the overall guidance of the MoH.

**Invasive bacterial vaccine preventable diseases (IB-VPD): Laboratory aspects**

The recommendations from the different meeting sessions are grouped below. In each discussion, it was recommended that a smaller technical laboratory working group should be convened to discuss relevant technical topics.

**Sentinel site meningitis laboratory diagnostics**

Different algorithms for testing CSF were explored, including the addition of a rapid Immunochromatographic test (ICT) for *Streptococcus pneumoniae* (Spn) which has increased the detection of Spn by up to 60-80% in culture negative CSF specimens in Bangladesh sentinel sites. The importance of PCR testing at the RRL was highlighted by the Gambia RRL which had identified Spn, Hib, or Nm in up to 50% of CSF culture negative specimens from sentinel sites in participating AFR countries.

- A standard algorithm for CSF specimen testing is required at sentinel sites and should be developed by a small working group of laboratories. WHO is working on developing laboratory posters on CSF specimen processing.
- All CSF specimens should be tested by a rapid test at the sentinel site with results provided to clinicians in a timely fashion in order to encourage clinician buy-in for surveillance.
- All CSF specimens should be frozen at the sentinel site and sent to the RRL for PCR testing.

**Regional Reference Laboratories**

The current roles and responsibilities of the RRLs were reviewed and discussed, with the following recommendations made:

- RRLs play a vital role in the network, and are agreeable to continuing to work with WHO in support of the IB-VPD network, which is an important public health global initiative.
- RRLs urged WHO to develop a more sustained funding stream, as the current one-year funding allocations prohibit the recruitment of staff and limit long-term planning.
- Further standardization is needed, and the draft laboratory manual for meningitis should be released as soon as feasible, along with the accompanying laboratory poster.
- The roles and responsibilities of the RRLs should be revisited, in order to provide further clarity in this regards.

**EQA/QC**

- The global IB-VPD EQA is an important component of the surveillance network, the NICD laboratory is well poised to continue implementing the EQA, and the EQA should be continued on an annual basis.
• The contact information used to report results back to the laboratory should be regularly updated and should include the WHO regional laboratory coordinator;
• Results of findings from individual laboratories should be provided as soon as possible, so that the laboratories and WHO can begin to plan appropriate follow up.
• The potential use of filter paper for the EQA should be explored.
• A global QC programme will not be launched, as Regional QCs monitored by ROs and RRLs are ongoing. The global EQA will to assess laboratory performance.

II e. Ad hoc technical advisory group closed session: next steps to improve IB-VPD surveillance
The ad-hoc group met following the surveillance meeting and noted that:
• Rotavirus surveillance network was functioning to a high degree, and producing important data for national decision making.
• WHO should focus on improving IB-VPD Tier 1 meningitis surveillance during the coming year.
• WHO should develop basic eligibility criteria for IB-VPD Tier 1 sites, and should provide support for as many sites as can meet those criteria.
  o Furthermore, WHO should then focus on a few selected sites to improve their performance capacity. This needs to be a transparent process.
• The purpose of the surveillance should be clearly articulated. In this regards, points should be included that the data is useful to Ministers to justify their budget requests for vaccine procurement and the capacity building component of surveillance
• More emphasis should be placed on engaging clinicians for IB-VPD surveillance.
III. FULL MEETING NOTES

III a. Global Update of the WHO new vaccines surveillance networks

Session: Tuesday, 13 September 2011

Session Objectives
• Welcome meeting participants and discuss the goals of the meeting
• Provide an overview of the planned introduction of new vaccines
• Provide an update on the global RV and IB-VPD surveillance networks and main activities, including:
  • An update on the status of implementation of action items from the 2010 global surveillance meeting
  • The quality of the data
  • Funding and staffing
  • Emphasizing the laboratory network

Overview of the planned introduction of new vaccines - C Mantel
There has been an increased global demand for and quicker availability of new vaccines. For example, Hib (Penta) vaccines have been introduced in 176/194 countries with introduction in India imminent; half of the world’s children currently remain unvaccinated but this will be markedly decreased following the planned upcoming Nigeria and Indonesia introductions. Fifteen new vaccines have been pre-qualified in the past year. A brief summary of the geographical distribution and introduction schedules of new and under-utilized vaccines (Hib (Penta), PCV, RV, HPV, MenA, Typhoid, JE) was provided. Achievements include: more projected funds available; more children vaccinated; increased applications/approvals; Menafri vac campaign. Challenges include: sustainability; accuracy of impact studies; prioritization of vaccine implementation.

Update on the global RV and IB-VPD surveillance networks, status of implementation of action items from 2010 surveillance meeting, and main activities - M Agócs and F Serhan
Update on RV network: Globally, 61 countries participated and reported data in 2010; clinical data was reported by 57/61 countries. Every region is well represented; the number of reporting countries has increased every year with the majority of countries GAVI-eligible. Over 47,000 children were enrolled during 2010. The monthly data related to rotavirus positivity demonstrates seasonality of RV. The data also shows that the median percentage of children hospitalized globally for gastrointestinal illness due to RV is ~40%. Overall, the RV network is robust and serves as a model network for informing decision making.

Update on the IB-VPD network: Globally, 49 countries participated and reported data in 2010, with all but one reporting clinical data. Overall, 73% of countries were GAVI eligible. Data was provided from 121 sentinel sites. There are large variations in number of enrolled suspected meningitis cases for Tier 1 (meningitis) surveillance
between countries. Tier 2 (meningitis/pneumonia/sepsis) surveillance was ongoing in 16 countries covering 4 regions during 2010. The observed proportion of children with a VPD (~1%) fell within the range of expected from other research (1-4%).

In general, there is a large variation in quality of Tier 1 IB-VPD data and WHO has identified a need to better standardize IB-VPD Tier 1 surveillance. In looking for ways to improve data management, WHO's strategic plan includes to place primary emphasis on improving Tier 1 surveillance during 2012, including: 1) Standardizing SOPs and tools (meningitis manual, global SOPs, clinical and laboratory posters, data management pamphlet, etc.), 2) Increased visits to sentinel sites including the laboratories for audits and/or on-site training, 3) Development of a matrix to prioritize next approaches. Feedback on the matrix of prioritized activities was sought from all participants during this meeting.

An overview of the structure of the global laboratory network and the status of action items from the 2010 global surveillance meeting was presented, as well as highlights of achievements and challenges.

**RV network:** 2010 rotavirus laboratory data was reported by 61 countries reporting as compared to 20 countries in 2009. Roles and responsibilities for RRLs include: 1) provide technical support to NLs and sentinel sites, conduct trainings, respond to queries and requests, distribution centre for primers and control reagents; 2) Participate in EQA and perform validation and confirmatory testing; 3) Conduct research (to be reviewed). The global distribution of rotavirus genotypes reported to WHO, in particular common vs. uncommon, needs to be further standardized. Highlights of implementation included: roles and responsibilities finalized; EQA panels developed and evaluated; validation/comparison of ELISA kits completed. In progress: standardizing laboratory procedures and laboratory supplies; assessment checklist for RRLs and NLs drafted (in folders); standard list of supplies (drafted). Next steps: Discussion about how to follow up and remediate issues with poor performing laboratories; Focus on standardizing SOPs.

**IBD network:** An overview of the structure was provided including all levels: GRLs, RRLs, NLs, and sentinel sites). *S. pneumoniae* (Spn) serotype data was provided by 5 regions in 2010 versus 2 regions in 2009. The number of countries with serotype data increased from 8 in 2009 to 28 during 2010. Action items 2011: Decision on rapid tests is necessary (Binax vs. latex agglutination); Should all cerebrospinal fluid (CSF) from suspected meningitis cases be frozen and sent to a reference laboratory for advanced diagnostic testing?

**III b. WHO closed session: development of criteria for receipt of IB-VPD surveillance funding, WHO staffing, data management, and laboratory**

Session: Sunday, 11 September 2011

**Session Objectives**
Discuss internally and agree upon:
- The IB-VPD matrix for Tier 1 and the criteria for receipt of funding
- WHO staffing requirements for new vaccines surveillance
• Data management:
  • Suggestion to include all reported VPDs in the twice yearly data collection process (and not just VPD in probable bacterial meningitis cases)
  • Agree on the method and frequency of revising data management tools;
  • Discuss what is needed to realize case based surveillance
  • Agree on Tier 1 meningitis case definition and review RV case definition
  • The role of RRLs, particularly in visiting and supporting sentinel sites

IB-VPD Tier 1 Matrix and development of criteria for receipt of IB-VPD funding
IB-VPD surveillance is not yet of high enough quality to serve the purpose of assisting countries with measuring vaccine impact. WHO will be held accountable in this regards, and future funding for surveillance is based on WHO's ability to improve surveillance quality. Senior WHO management staff place a high priority on IB-VPD surveillance.

WHO will develop minimum criteria for countries to meet in order to be eligible to receive WHO funds for IB-VPD surveillance. Discussion criteria of potential criteria included:
1) MoH focal point identified and in place
2) Sentinel site focal points identified and in place
3) Countries are enrolling at least 100 suspect meningitis cases per year
4) Country is identifying VPDs
5) Country plans to introduce PCV (and possibly RV, meningitis, penta)
6) Countries that are already in the surveillance network and reporting data.
7) Preference will be given to countries conducting both RV and IB-VPD surveillance.

It was specifically noted that countries should be notified well in advance of the establishment of these criteria, and due consideration should be given to countries joining the network to ensure adequate time to meet the criteria. Additionally, some countries may have difficulty to meet point 3 above, but should not be dropped from the network while the country was making efforts to improve their system. Since some countries do not have a national laboratory, this specific criteria would not be included.

WHO Staffing
WHO RO and HQ staff met to review the status of the surveillance networks and agree on key activities to improve the network. ROs and HQ face the challenge of limited staffing, both professional and administrative, in some particular offices which hampers the development of the network. ROs will share this information with HQ, and WHO will work to resolve this issue.

Data Management
1) Agreement to share information on all VPDs detected, not just those found in probable bacterial meningitis cases.
2) The data collection tool will be assessed each year during the global surveillance meeting to determine if any changes are required. It will only be revised following this process.
3) Agreement on transition to case-based IB-VPD surveillance, pending adequate WHO staffing and agreements on safe-guarding of the data
WHO will move towards a case-based system for IB-VPD surveillance, pending adequate WHO staff to develop the required technical infrastructure, and the development of appropriate processes to ensure the safe-guarding of data. No personal identifiers will be shared.

4) Agreement on case definitions: the following case definitions were agreed:

- **Rotavirus: Suspect Case**
  Any child aged 0-59 months admitted for treatment of acute (i.e. ≤14 days) watery gastroenteritis/diarrhoea to a sentinel hospital conducting surveillance. Excluded are children with bloody diarrhoea and children transferred from another hospital.

- **IB-VPD: Meningitis**
  **Suspect Case**: Any child aged 0-59 months admitted to a sentinel hospital conducting surveillance with sudden onset of fever (>38.5°C rectal or 38°C axillary) plus a history of one of the following signs: neck stiffness, altered consciousness with no alternative CNS diagnosis, or other meningeal sign

  OR

  Every patient aged under 5 years of age hospitalized with a clinical diagnosis of meningitis.

  **Probable Case**: A suspected meningitis case (as defined above) with CSF examination showing at least one of the following:
  
  1) Turbid appearance;
  2) Leukocytosis (> 100 cells/mm$^3$);
  3) Leukocytosis (10-100 cells/mm$^3$) AND either an elevated protein (>100 mg/dl) or decreased glucose (< 40 mg/dl)

  Note: if protein and glucose results are not available, diagnose using the first two conditions (i.e. turbid appearance or leukocytosis > 100 cells/mm$^3$)

  **Confirmed Case**: A suspected meningitis case that is laboratory-confirmed by growing (i.e. culturing) or identifying (i.e. by Gram stain, antigen detection, PCR or other methods) a bacterial pathogen (Hib, pneumococcus or meningococcus) in the CSF or from the blood in a child with a clinical syndrome consistent with bacterial meningitis

**Laboratory**

- Agreement that the current EQA for RRLs will be continued and that the planned global QC programme with samples sent from RRLs to GRLs is not needed at this stage as the EQA is sufficient to assess the RRLs capacities.

  This issue was further discussed during the surveillance meeting with agreement to continue the global EQA but to limit the QC to the direction of the ROs, as deemed appropriate by the ROs. The privacy of countries should be maintained to the highest degree possible.

- Agreement that the existing IB-VPD laboratory assessment questionnaire is appropriate for RRLs, but should be shortened for sentinel site assessments. HQ will work to shorten the assessment questionnaire and share with ROs for input.
• Agreement that clearer protocols are required to guide which RV specimens are sent to RRL for genotyping (to be aligned with the RRLs capacities and reporting to WHO ROs).
  
  HQ will work to develop a protocol and share with ROs for input.

III c. WHO Data management: Defining data management issues and next steps forward to streamline the system

Session: Monday, 12 September 2011


Session Objectives

• For each RO and HQ, review the existing data management structure, and discuss the strengths, and weaknesses
• Determine if the RO maintains case-based or aggregated data
• Identify a limited number of achievable priority activities to improve the WHO data management structure during 2012

Regional Offices and HQ review of existing data management systems:
AFR, AMR, EMR and WPR presented their data management system. The data manager from EUR was unable to attend and the SEAR data manager’s position is currently vacant. All four regions developed a database system to use at country and regional levels. Data collection is monthly in AFR and EMR, while it is quarterly in WPR. AMR has an online data collection system with continuous possibility for update. All regions reported that data is analysed frequently and widely used. The major weaknesses identified in most regions are the weak data management structure at the country level and problems in the quality of the data reported.

Improving data quality
Priority actions were identified, in order to improve the quality of the data reported and strengthen the data management platform:

• Minimize revision of variables and data collection template. When revision is necessary, revise variables during a consensus meeting and allow time to implement changes. The minimum period between revisions should be 2 years.
  o The current template and list of variables will be revised after the surveillance meeting to include reporting of VPDs in suspected meningitis cases (Spn, Hi, NM) as well as probable bacterial meningitis cases.
  o This above template will be used for the next 2 years
• Reporting deadlines and timelines from ROs to HQ will be modified as follows:
  o The current reporting periods will be maintained (May and November.) However, data reported in November will include the previous year’s data and the first 6 months of the current year.
  o Data reporting: time periods and frequency from RO to HQ:
    o 1) May: January to December data of the previous year
    o 2) November: January to June of the current year and the previous year’s data.
Firm deadlines will be set up for the data that will be included in the bulletins. Data received after the deadline will not be included in the bulletin.

Additional staff are needed, especially:
- For data management functions at the sentinel site.
- Data management functions at the national level.

Data quality should be improved by:
- Promoting regular data review meetings with national MoH and sentinel sites, involving surveillance and laboratory coordinators and data managers.
- Regular training of data managers at sentinel sites/national levels that include points beyond data management, such as basic issues regarding surveillance.

Improved communication on how the data is used in order to improve the motivation at the sentinel site.
- Consider translating the global bulletin into other languages (Spanish, French, etc.)

Continued and enhanced collaboration between regional offices and HQ should be undertaken, and should include a parallel session on data management at the next global surveillance meeting.

In addition, more broad based recommendations included:
- Organize regular training of data managers at sentinel sites/national levels (beyond data management, i.e. basic issues on surveillance).
- Promote regular data review meetings with national MOH and sentinel sites, involving surveillance and laboratory coordinators and data managers.
- Improve communication on how the data is used in order to improve motivation at the site level. One option would be to have the Global Bulletin translated in other languages (Spanish, French).
- Ensure that one person who is directly responsible for ensuring that all components of surveillance are working (including but not limited to data management) should be dedicated to each sentinel site.

Sharing IB-VPD case-based data with WHO HQ:
Four of six Regions have case-based data for Rotavirus and IB-VPD: AFR, EMR, EUR and WPR. AFR, EUR and WPR accepted to share the case based data with HQ. Decision is pending for EMR.
It was agreed that prior to sharing the case base data the following issues have to be addressed:

- Agreement from all partners, with a statement on how the data will be used
- Agreement on a standardized system for data sharing
- Definition of the set of variables: the regional offices will share with HQ their variables and a common set, corresponding to HQ needs will be identified.
- Adequate staffing to complete the technical steps required.

Other comments during discussion: Regional attendees stated that there was a lack of clarity around new formats; the participants were concerned about continual changes made. The group discussed ways to improve grassroots level work/involvement, and suggested that surveillance bulletins be distributed at each reporting level. An improved sense of priorities was required as there is currently too much competition for attention/work along with inadequate resources.

**III d. Rotavirus surveillance: Ministry of Health management, clinical and other aspects**

**Session:** Tuesday, 13 September 2011

**Objective:** To highlight the rotavirus surveillance network, as an example of a surveillance network that is generating good quality data that is being used:
- by MoH for decision making to introduce new vaccines
- by MoH and others to measure vaccine impact
- by WHO and partners to optimize RV vaccine schedules

**Paraguay: establishing rotavirus surveillance and using data to make decisions regarding vaccine introduction.** Dr. S. Arza
Paraguay introduced monovalent rotavirus vaccine (RV1) with 2 doses given at 2 and 4 months of age in January 2010. By end 2010, rotavirus vaccine coverage was 69% for the first dose and 60% for the second dose. Rotavirus surveillance was initiated in 2004 at 4 sentinel sites each performing ELISA testing. Molecular testing is performed at the Laboratory Central Salud Publica. Surveillance data has shown that the rotavirus disease in Paraguay is seasonal with annual peaks in July to September. From 2004-2010, approximately 20% of diarrhoeal disease was due to rotavirus. In the pre-vaccine era, the greatest disease burden occurred among children <12 months of age with approximately a third of the disease severe. Very preliminary data from the post-vaccine period suggests that the disease may be shifting to older age groups with only 25% of disease classified as severe. G2, G4 and G9 genotypes were commonly circulating in the pre-vaccine era.

The rotavirus surveillance system has numerous strengths including committed human resources, active surveillance centres, and an epidemiological reporting form that collects specific data to determine disease burden. Over the surveillance period, laboratory capacity has strengthened. Because surveillance was initiated 6 years prior to vaccine introduction, solid and stable baseline information is available that captures the year to year variability of rotavirus disease. Weaknesses in the surveillance system also exist with a limited number of trained human resources, poorly completed notification forms, insufficient integration of the epidemiology and
laboratory components of the network, and insufficient characterization of genotypes.

Many lessons have been learned regarding the technical, programmatic, and financial support needed for introduction of rotavirus vaccine in Paraguay. Vaccine purchase was possible due to the PAHO revolving fund. However, vaccine introduction required coordinated technical and political efforts. Evaluations that should be undertaken before introduction of any vaccine include cost-effectiveness studies as well as analysis of logistical considerations including vaccine storage, transport, adverse events, cold chain capacity, vaccination card collection, and adverse events considerations. Feedback to sites and involved partners is critical and as well as surveillance integration to measure the true impact of vaccine.

**The Sudan: decision making, monitoring, and measuring impact** - A Mostafa

Diarrhea is the 4th most common cause of hospital admissions and 5th most common cause of in hospital deaths among children <5 years of age in the Sudan. Sudan initiated rotavirus surveillance in April 2007 in collaboration with the MoH, EMRO, and NAMRU3. Eight sentinel sites were initially selected but reduced to five in 2011. The rotavirus surveillance system follows the WHO SOP. Three focal persons are based at each site: clinical focal person, laboratory coordinator, chief nurse. Additionally, at the national level, there is a national data manager, a national laboratory focal person, and a national surveillance focal person. The MoH is responsible for coordinating the planning, capacity building, data management, and monitoring and evaluation for the surveillance network. Planning includes incorporating surveillance as part of the cMYP, preparing the annual plan of action, estimating budget and supplies needed. The MoH coordinates with partners, senior paediatricians in the sentinel sites, and the national public health laboratory. For data management, the MOH prepares, prints, and distributes forms and registers, reviews weekly gastroenteritis cases reported from selected sites, processes and analyses the data monthly, and provides feedback and feed-forward to the sites. To build capacity, the MoH provides refresher trainings to clinical staff, training on laboratory testing, basic training for new focal persons, orientation sessions for medical doctors during supervisory visits, strengthens infrastructure of laboratories, and supplies laboratory materials and supplies. Monitoring surveillance activities include review of data in weekly surveillance meetings, monitoring of focal persons through reporting performance indicators, regular supervision visits, and an annual review and evaluation meeting. In the latest performance review the sites had an aggregate performance score of 87% (range: 75%-96%). Only 1 site failed to achieve a passing score of >80%. Over the entire surveillance period from April 2007 to July 2011, there were 11135 stools collected with 3305 testing positive (34.6%). The G2P[4] genotype was the most commonly detected genotype during the last two surveillance years. Quality control supervision by NAMRU3 found that the testing was performed adequately.

Prior to the availability of surveillance data, the decision to introduce new vaccines was based on regional estimates, limited national data, and gray data. After the establishment of the rotavirus surveillance network, the decision to introduce rotavirus vaccine was based on surveillance data that showed the high burden of rotavirus disease in the Sudan and resulted in the
prioritization of rotavirus vaccine introduction over pneumococcal vaccine introduction. Rotavirus vaccine was introduced in the Sudan in July 2011. Surveillance data will further be used to measure the impact of rotavirus vaccine on rotavirus disease burden. To measure vaccine impact, vaccination status was added to case report forms and training was conducted on how to collect the data.

Strengths of the surveillance system include leadership by the MOH, establishment of rotavirus testing at three of the sites, clearly defined SOPs and roles and responsibilities, capacity building of the national laboratory personnel and infrastructure, and the availability of data for monitoring vaccine impact. Challenges and constraints of the system include expanding testing to all sites, high turnover of focal persons, supply management, shipping of specimens to the reference laboratory and shipping of kits to the sites, and collection of accurate vaccination status. This was the first time in Sudan that the decision to introduce a new vaccine was based on scientific evidence. The surveillance system has improved in performance and quality and will enable the monitoring of rotavirus vaccine impact. Investment in disease surveillance for decision making is worthwhile. The rotavirus surveillance network will continued to be strengthened and maintained to enable the monitoring of rotavirus vaccine impact. Furthermore, the network will be expanded to include other vaccine preventable diseases.

South Africa: decision making and measuring impact. Dr N Ngcobo

Diarrhoea is a major cause of morbidity and mortality in South Africa. Diarrhoea accounts for 24% of all deaths among children <5 years of age with rotavirus diarrhoea responsible for approximately one third of these deaths. From 2006-2008, sentinel rotavirus surveillance found that rotavirus accounts for 25% of all diarrhoeal disease. Rotavirus occurs year round with a seasonal peak in autumn and winter. The high incidence of HIV was an initial concern regarding vaccine safety but studies have since shown that it is safe and effective in HIV infected and malnourished children.

The decision making process for a new vaccine introduction in South Africa is multilevel. First, the National Advisory Group on Immunization (NAGI) reviews data regarding the new vaccine and makes recommendations to the National Department of Health which in turn sends the recommendation to the National Health Council (NHC), a body with all ministers and heads of health from the nine provinces. Once the NHC approves, the recommendations are taken to the Ministry of Finance for funding and a budget is allocated. NAGI recommendations are not legally binding and NAGI is not concerned with programmatic issues. Vaccine introduction was delayed due to changes in the vaccine formulation and was rolled out nationally in August 2009 following the initiation of surveillance in April 2009. Budgets have been a problem for vaccine rollout with a budget shortfall within the first two years. The vaccine manufactures provided added value through support for training, cold chain, surveillance, and social mobilization.

There are five main approaches to outcome and impact measure including estimating rotavirus vaccine coverage, sentinel surveillance for diarrhoeal disease, disease burden studies, diarrhoeal disease burden monitoring using routinely collected data, and ongoing mortality studies. Rotavirus vaccine coverage has
steadily increased from 2009 to 2011. Despite low vaccination coverage at the five sentinel sites (53-58% one dose coverage and 40-45% two dose coverage), a notable decrease of 62% was observed in rotavirus diarrhoea among children <1 year of age and a 34% decrease was observed in 1 year olds resulting in a 54% decrease in rotavirus disease among all children <5 years of age. The start of the rotavirus season was also delayed in the post-vaccine introduction era compared to the pre-vaccine era. Routinely collected data on diarrhoeal disease showed that incidence of all-cause diarrhoeal disease decreased in almost all of the 9 provinces following vaccine introduction. Challenges still remain including low vaccination coverage and stock outs and all-cause diarrhoea incidence is only available for <5 year olds and not <1 year olds. Long term trends will need to be monitored, herd effects evaluated, and genotypes continued to be monitored. The public response to the vaccines has been positive and sustainability of the rotavirus vaccine needs to be assured. Rotavirus vaccine coverage should be increased further, surveillance continued, and work with suppliers and provinces performed to ensure adequate supply and eliminate stock outs.

**Americas Region: Assessing rotavirus vaccine impact.** Dr. L. Olivera

Fifteen countries, including 4 GAVI-eligible countries, and 1 territory have introduced rotavirus vaccine in the PAHO region since 2006.

**El Salvador** is a low middle income country that introduced monovalent rotavirus vaccine (RV1) in October 2006. Rotavirus surveillance was established in January 2006 at 7 sentinel hospitals representing 48% of the annual admissions for diarrhoea among <5 year olds. A case-control study was carried out from January 2007 to June 2009 to evaluate the effectiveness of RV1 in routine use using the WHO standard protocol. Cases were identified from 7 hospitals within the surveillance system and three date of birth matched controls were selected for each case. Two doses of vaccine were 76% effective against rotavirus diarrhoea hospitalization, one dose was 51% effective. Two doses of vaccine were 83% effective among 6-12 months olds and 59% among children >12 months old. Between January 2006 and June 2009, 33% of children <5 years of age who were enrolled in the surveillance system were positive for rotavirus diarrhoea with 98% of these cases detected between January and June. In 2006, when no vaccine was available, 62% of children <5 years of age tested positive for rotavirus diarrhoea during the January to June season. During the 2007 rotavirus season, vaccine coverage was 58% and 49% of children were rotavirus positive. During the 2008 rotavirus season, vaccine coverage was 83% and 16% of children were rotavirus positive. During the 2009 rotavirus season, there was a vaccine shortage and vaccine coverage fell to 61% and the proportion of children positive for rotavirus rose to 40%.

**Nicaragua** is a low middle income, GAVI-eligible country that introduced pentavalent rotavirus vaccine (RV5) in October 2006. A case-control study was carried out from June 2007 to June 2008 to evaluate the effectiveness of RV5 in routine use using the WHO standard protocol. Cases were identified from 4 hospitals that initiated surveillance at the study’s start. Individually matched hospital and neighbourhood controls were selected for each case. Three doses of vaccine were 49% effective
against rotavirus diarrhoea requiring hospitalization or IV rehydration, 58% effective against severe diarrhoea, and 77% effective against very severe diarrhoea.

Bolivia is a low middle income, GAVI-eligible country that introduced monovalent rotavirus vaccine (RV1) in August 2008. Rotavirus surveillance was established in January 2006 in 6 hospitals. A case-control study was carried out from March 2010 to July 2011 to evaluate the effectiveness of RV1 in routine use using the WHO standard protocol. Cases were identified from 6 hospitals within the surveillance system and three date of birth matched controls were selected for each case. The percent of children <5 years enrolled in surveillance who tested positive for rotavirus diarrhea was 39% in 2006, 40% in 2007, 49% in 2008, 36% in 2009, and 27% in 2010. Two doses of vaccine were 75% effective against severe rotavirus diarrhea and one dose was 45% effective.

Data from rotavirus surveillance networks can and should be used to monitor vaccine impact. Case-control studies and pre-/post-vaccine introduction studies can been done using surveillance data of good quality. Scientific studies can be used to stimulate MoH officials and gain support for the vaccination program.

**Using rotavirus surveillance data to optimize vaccination schedules.** C. Sanderson

Surveillance data can be used to inform and improve vaccination schedules. To have the most effective vaccination program, the timing of vaccine administration must be such that it is not given too early so that it is less effective or too late so that disease has already occurred. The age distribution of rotavirus cases is important in determining the optimal schedule to prevent the greatest amount of disease. This work has thus been launched to determine the optimum vaccination schedules. Data was eligible for inclusion in this analysis if it included >100 subjects who were <3 years of age with <= one month age bands available for children <1 year of age. Data were available for 38 populations with a median of 665 events and 85% from hospital admissions and 5% from surveillance. Most testing was by ELISA. In populations with cases of disease early in life and delayed vaccination coverage, fewer children will be protected by the vaccination program. Wealth quintiles also have influence vaccination coverage and age distribution of cases. Surveillance data are essential for these analyses especially if population based with a sufficient number of children enrolled using consistent methods. More data are needed on efficacy of different doses as well as on age specific efficacy. The analyses should be repeated by socioeconomic status and implications for risk of intussusceptions should be incorporated.

**Next Steps to enhance rotavirus surveillance:**
- Support MoH oversight and guidance of sentinel surveillance activities
- Document the experiences shared in the session so that other countries could benefit from these lessons learned
- Data from rotavirus surveillance networks should continue to be used
  - For decision making in new vaccine introduction
  - To measure vaccine impact
  - Address questions of vaccine performance
• Continued support of rotavirus surveillance networks is urgently needed to
  ensure the availability of high quality data
• Countries planning rotavirus vaccine introduction should look to countries who
  have already introduced for lessons learned

III d. Rotavirus Laboratory Network Sessions

Session: Monday, 12 September 2011

Session Objectives
• Network management and updates: Provide meeting attendees with an
  overview of the rotavirus surveillance network at HQ and RO levels, with a focus
  on the laboratory
• Review the current roles and responsibilities of each level of laboratory in the
  network (sentinel, national, regional, and global)
• Determine the current needs including training of RRLs in order to fulfil the
  stated roles & responsibilities of RRLs
• Review the experience of the global EQA and planned QC, and revise the
  strategy as needed for 2012

HQ update: rotavirus surveillance network and funding - M Agocs, F Serhan

Overview of the rotavirus surveillance network epidemiology and finance sides.
The number of countries reporting to WHO system has increased every year. In
2010, 61 countries reported data to the WHO network during 2010, with good
representation from each WHO region; the majority of countries were GAVI eligible.
Clinical data was reported by 57/61 countries. Overall, 47,508 children <5 years of
age were enrolled in the WHO system in 2010. The range of enrolled children varied
from 31 to 6461 by country. Monthly data demonstrated seasonality of RV disease.
The data indicated that the median percent of children hospitalized globally for
gastrointestinal illness due to RV was ~40% during 2010.

Implementation status of recommendations from 2010 Global Surveillance meeting.
Forty-six action items were recommended at the 2010 Global Surveillance meeting
for both IB-VPD and RV networks. Highlights to implementation status were
included in meeting folder. 18 actions items were completed (39%), 22 (48%) are in
progress or partially met, 3 (7%) not met and 3 (7%) deferred or not feasible.
Examples of action items completed included:
• Summarize RV data for WER/MMWR
• cMYP revised to better reflect new vaccines surveillance
• Roles and responsibilities of GRL, RRL, NLs and SSL finalized
• EQA PT panels developed at GRL and evaluated at RRLs
• Forum for regional and global information exchange (surveillance meeting)
• Validation of RV kits (ProspecT, Rotaclone comparison at GRL completed
  and Ridascreen in progress)
Action items In progress include:
• Audit/assess sites:
  o RV: 14 (8%) of 175 sentinel sites
  o IB-VPD: 29 (24%) of 121 sentinel sites
• Standard lab procedures (available SOPs from WHO regions and Rotavirus lab manual)
• Assessment checklists for RRLs and NLs (drafted)
• EQA and QC
• Standard list of supplies (drafted)
• Comparison of regional typing strategies (information being collected)

Not met (only lab issues):
• Standardizing training modules (based on WHO RO available ones) : to be further discussed during the meeting

Deferred or not feasible action items include:
• Data management
  – RO will transition to transmitting data to HQ on a monthly basis using agreed data exchange format
  – HQ will transition to providing internal feedback to RO on a monthly basis
These two items were not completed as the existing data management capacity was insufficient to do so.

Overview of the WHO Rotavirus laboratory network - F. Serhan

Network structure: Ten RRLs exist and are distributed in the 6 WHO regions to provide technical support to national and sentinel site labs. WHO works closely with a Global Reference Laboratory (GRL) at CDC Atlanta to provide technical support to regions and to monitor the global EQA programme. WHO coordinates the networks and has assigned laboratory coordinators at HQ and in ROs. Responsibilities of laboratory coordinators include monitoring lab performance, coordinate QA/QC programmes, organize lab trainings/assessment visits and facilitate procurement of laboratory supplies.

RV lab data: Global distribution of RV genotypes:
The number of countries reporting genotypes has increased from 20 countries in 2009 to 37 countries in 2010. Approximately 5000 RV genotypes were reported to the WHO system in 2010. P[8], G1 and P[4], G2 represent the largest percentage among the common genotypes with 31% and 10% global distribution respectively. Since 20% of genotypes fell in the "uncommon" category based on the current WHO classification, there is a need to review the current classification of common vs uncommon genotypes. The distribution of uncommon RV genotypes by region was 55%, 35% and 31 % of genotypes in SEAR, AFR and EMR respectively, which highlighted again the need for regional comparison of data and new classification of genotypes.

Overall, RV network is robust and serves as a model network for informing decision making. Considerable achievements have been made on the lab side.

AFR update: regional rotavirus surveillance network - J Mwenda
Seventeen countries participate in the AFR rotavirus surveillance network and 20 sites report data to the WHO system. During 2010, 88% of children had a stool specimen collected, and 42% were RV ELISA confirmed cases. Genotyping was performed for 708 cases, with 35% with uncommon genotypes. The two most common genotypes were G1[P8] at 14.5% and G9[P8] at 13.6%. AFRO organizes regional training activities at the RRLs. The last training on genotyping was held in Medunsa RRL in South Africa, June 2011. Challenges include lack of full MoH ownership, turn over of trained staffs, SOPS and lab manuals not strictly used, competing priorities within the programme and minimal genotype data from 2 RRLs. Main achievements are the increased awareness and clinical management, and evidence based decision making. Thirteen countries will receive GAVI support to introduce RV vaccines and for capacity building.

AMR update: regional rotavirus surveillance network - L Oliveira
Fifteen countries in AMR have introduced RV vaccine, and 16 countries are part of the RV AMR surveillance network with 86 sentinel sites. The percent of RV positive cases is decreasing with the increased number of countries introducing RV vaccines. Genotyping results showed G1[P8] and G2[P4] as the most common strains in 2010 with 47% and 39% representation respectively. AMRO has complete "new vaccines field guides" that are available in English and Spanish and include guidelines on sentinel site surveillance, case definition and classification, laboratory techniques, evaluation indicators and steps for new vaccines introduction. The most recent RV surveillance latest activities in AMR include genotyping training for lab personnel at RRLs, short time consultancies to countries for both epidemiology and laboratory sides, Regional Surveillance Meetings of New Vaccines held every 2 years since 2005, supply of ELISA kits for almost all countries, as well as support and supervision of national action plans.

EURO update: regional rotavirus surveillance network – D. Videbaek
Rotavirus vaccine has been introduced in Austria, Belgium, Finland, Israel, and Luxemburg. Six countries (Azerbaijan, Georgia, Tajikistan, Ukraine, Moldova and Armenia) participate in the EURO rotavirus surveillance network and are supported by a RRL in Minsk, Belarus. Specimens are tested for rotavirus at a national laboratory, and all laboratories send specimens to the RRL twice a year for QC and genotyping. The EUR RRL participated in the first phase of the global EQA and scored 100%. The number of rotavirus confirmed cases upon retesting of ELISA positive samples at the RRL has improved in 2010. G1P[8] was the most predominant genotype. There is only a small % of untypeable strains (before sequencing). EuroRota software for surveillance has been implemented and is used in all 6 participating countries. The data is entered in the software at National level. EUR sends all the untypeable samples to GRL for typing.

Problems and challenges included that the WHO recommended Oxoid ProsPecT kit and some plastic wares for specimen collection are not available for purchase locally. EURO cannot distribute PT panels to network laboratories using dry ice. It has been planned to conduct site monitoring visits to Georgia and Ukraine laboratories. The scientists at RRL need more training in sequencing to genotype rotavirus strains. Some genotyping reagents should be included in GSM catalogue.
SEARO update: regional rotavirus surveillance network - P. O’Connor
Four countries participate in the RV surveillance network (Indonesia, Myanmar, Nepal and Sri Lanka), and are supported by a RRL in Vellore, India. India has conducted RV surveillance for the last 3 years but Indian rotavirus cases are not integrated in the WHO network. There is a potential to expand the number of sentinel sites in SEARO. Problems and challenges include the lack of data flow between national government and WHO country offices. The sites conducting both IB-VPD and rotavirus surveillance could further synergize their efforts.

WPRO update: regional rotavirus surveillance network - K. Fox, F Paladin
Currently 7 countries (Cambodia, China, Fiji, Laos, Mongolia, Papua New Guinea, and Vietnam) participate in the RV surveillance network and are supported by 3 RRLs- MCRI Australia, Korea CDC and China CDC. MCRI and KCDC participated in first EQA panel testing. KCDC also had an on-site assessment of baseline laboratory capacities and practices. The national laboratories send samples to RRLs twice a year for QC. In 2010 a total of 4791 samples were tested positive for RV out of which 1364 (55%) were sent for genotyping. Overall, 98% of samples were confirmed as ELISA positive by RRL and 88% were confirmed ELISA negative by RRL. G1P8 (35.7%) was the most predominant genotype in 2010 followed by G2P4 (28.5%). All the non-typeables were sent to National laboratories with sequencing capacity. Several hands on trainings took place in 2010 to train KCDC and China CDC staff. A RRL RV database has been created which provides automated generation of reports.

Problems and challenges include obtaining a correct count of eligible cases, delay in testing by RRLs due to long process at custom clearance, and that the surveillance laboratory database needs training and monitoring after implementation. Further efforts are required to standardize the case definition, document lessons learned, obtain more genotyping data, conduct more onsite visits and assessments, distribute standard supplies to RRLs, develop easy shipping processes for EQA and QC possibly including lyophilization, and developing criteria for sentinel site selection.

Rotavirus External Quality Assessment programme (EQA) - M Bowen
The global EQA programme was launched by CDC GRL in 2011 with a panel of 8 samples (positives and negatives) with common representation of G and P genotypes shipped on dry ice to 9 RRLs and 2 referee laboratories. The average cost of shipment was $1492.45. The passing score for EIA and genotyping is 80%. EIA results were: of the 9 RRLs, 8 laboratories passed and 1 laboratory failed. Both referee laboratories achieved a passing score. EIA kits used by different laboratories were Rotatclone, ProsPecT, Ridascreen and Biotracer. The RRL who failed the EQA testing had used Ridascreen kit for EIA. Genotyping results were: out of 9 RRLs, 7 passed the genotyping and 2 failed. One RRL who failed had stored the samples at 4°C for long time. Challenges in further improving the EQA included that lyophilization of samples did not work. PT panels stored at 4°C and room temperature for 30 days showed good EIA results but not good genotyping results. In expanding the global EQA to national and sentinel laboratories, dry ice shipments are not feasible. Temperature stability studies of PT panels are under way to determine if the second EQA round should be done at 4°C or room
A follow up plan should be developed for laboratories which failed EQA testing, with a possible next step for non-passing laboratories would be to perform testing on a second panel. Drafts of checklists to assess RRLs and National labs were shared before the meeting with ROs laboratory coordinators. Checklists will be finalized after comments are received in October 2011.

**Rotavirus Quality control strategy** - R Gautam

A proposal was shared for RRLs to select a panel of 50 stool specimens for EIA and genotyping studies at the GRL for QC. The GRL would then perform EIA on the 50 samples provided by each RRL and genotype 10 samples identified by each RRL. However, all RRLs and WHO agreed that QC of sentinel and National laboratories is already done twice a year by the RRLs so there is no need for additional QC by GRL. Rather, the EQA panel testing is sufficient to judge RRL capabilities.

**Standardizing Procedures and Supplies.**

**Objectives**
- Review the current use of standardized operating procedures (SOPs) in the network, including for strain characterization, and the use of supplies
- Determine for which activities (e.g. specimen collection, storage, processing and use of kits) SOPs are needed and for which activities additional guidance (rather than SOPs) would better help to direct the network

**Standardized SOPs for Rotavirus Surveillance Network:** M Bowen

Standardizing SOPs can promote uniformity in testing procedures, facilitate trainings and provide guidance for areas where methodologies have been optimized for each region, i.e. genotyping. However, standardization of SOPs has cons as laboratory practices vary between regions and should thus be regionally optimized. The current WHO RV laboratory manual provides an SOP, but other SOPs are needed for specimen collection, transport, processing and storage, diagnostic immunoassays with new available kits (e.g. ProspecT, Rotaclone), PCR, sequencing and data analysis. There is also a need for a standardized list of supplies. A draft list was shared with ROs before the meeting for comments. The list should be finalized and submitted to the WHO catalogue to facilitate procurement process.

**Summary of Meeting of Rotavirus Laboratory Network**

**Session Objectives**
- Review the main meeting discussions
- Discuss next steps with recommended action items to be completed prior to next surveillance meeting in 2012

The following recommendations were made:
1. Further standardization is required to:
   a) determine which genotypes are truly 'uncommon' and which are 'untypeable';
   b) ensure the agreed global case definition is being used2; and

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2 Rotavirus: Suspect Case: Any child aged 0-59 months admitted for treatment of acute (i.e. ≤14 days) watery gastroenteritis/diarrhoea to a sentinel hospital conducting surveillance. Excluded are children with bloody diarrhoea and children transferred from another hospital.

Report of 2011 Global New Vaccines Surveillance Meeting
c) clearly define roles and responsibilities of all the partners
2. Document lessons learned, particularly for AMR, so that countries introducing vaccine in other regions can benefit.
3. More genotype data is needed as vaccine is being introduced globally.
4. Critical supplies should be assured.
5. On site visits and assessments should be conducted, with recommendations provided to improve the quality of work.
6. MoH and WHO should integrate RV and IB-VPD surveillance as possible.
7. Continue the global EQA and regional QC systems in order to monitor performance, however, a simpler process would be advantageous, such as lyophilization and hand carrying of panels/specimens.
8. A global QC programme would be duplicative with the regional QC that are monitored by the RRLs and should not be launched. The global EQA will provide sufficient information on the RRLs capacities.
9. A follow up plan should be developed for laboratories that fail global EQA / regional QC.
10. Focus in consolidating the network, rather than expanding it.
11. Create a technical working group to discuss in depth the laboratory issues.

III e. Status of IB-VPD surveillance and potential actions to improve quality of Tier 1 meningitis surveillance through MoH management, clinical, and other aspects

Session, Tuesday 13 September 2011

Session Objectives
- Outline major potential issues contributing to poor quality Tier 1 data
- Summarize potential activities to pursue during the next 12 months to improve Tier 1 data quality
- Review the status of the IB-VPD surveillance in each WHO Region, with regards to management, epi/clinical, laboratory and data management issues, and to describe the needs in the coming year.
- For each WHO Region, receive input on the matrix of potential activities to improve IB-VPD surveillance, particularly which activities are the highest priority

IB-VPD Tier 1: Matrix Overview - M Agócs
Currently 49 countries are conducting Tier 1 surveillance and 16 countries are conducting Tier 2 surveillance as part of the IB-VPD surveillance network. WHO has developed a matrix to outline potential activities, both managerial and technical, that could improve the quality of IB-VPD Tier 1 surveillance. The Matrix was developed based in part on participant survey responses at the 2010 new vaccines surveillance meeting and also with inputs from an informal technical advisory group. The Matrix is meant to be used as a tool to prioritize which activities could have the highest impact, while taking into account the amount of time required to implement those activities. Sentinel site visits appear a high priority but are time-intensive. WHO needs feedback on appropriateness/completeness of elements in the Matrix. For CSF specimen processing, improving diagnosis is a high priority; the network (RRLs) needs to evaluate use of new technologies. More regular meetings/communications may be needed, as there have been too many specific
issues to address during annual meeting. On Wednesday, the closing session is designed to receive feedback the Matrix from meeting participants.

**IB-VPD Surveillance, WPR Overview - K Fox**
Currently WPR sites are mostly Tier 1 (hospital-based meningitis surveillance), except for Mongolia (all hospitals) which are conducting Tier 2 surveillance. In several sentinel sites the reported number of suspected cases is less than the WHO proposed minimal number for IBD surveillance. Management of surveillance is in the national EPI programme or is transitioning from national laboratory to national EPI (Philippines, Viet Nam). Current challenges to good IBD surveillance: variable case definitions; variations in percent probable bacterial meningitis with confirmed bacterial etiology (Sp, Hi orNm) between countries, differences in clinical threshold for lumbar puncture (enrolment takes place only for cases with a CSF specimen, and thus the percent of cases with lumbar puncture is not a meaningful indicator in these sites); previous antibiotic use; adequate volume of CSF; timeliness of transport to laboratory; some variations in standard forms and databases (Mongolia pneumonia and PNG); Promising preliminary results have been obtained with the addition of Binax for Spn detection in PNG.

**IB-VPD Surveillance, SEAR Overview - P O’Conner**
SEAR has history of IBD surveillance (INCLLEN) and high functioning, population-based surveillance sites in Bangladesh but MoH ownership is weak as these sites were established as research sites. Thus, the MoH/EPI should be involved more to make them aware of the existing data. The low positivity for bacterial cultures makes rapid diagnostic alternatives a priority. Critical issues are human resources (WHO surveillance, data, laboratory personnel), funding for sentinel sites and RRLs, and supervision. For the sustainability of network, integration with other, more-established VPD surveillance (polio, measles, JE) should be considered. Developing informal networks with additional research sites/institutions could incorporate sites with high quality data (i.e., IBD sites in India) without enrolling additional sites in network. Advocacy is needed for surveillance to make use of available data, and to generate data where needed for decision-making. For a region with such a large population, network expansion should be considered to cover more of the population.

**IB-VPD Surveillance, EUR Overview - AM Wasley**
EUR has 3 Tier 1 sites and a RRL in Russia. The surveillance network is limited to GAVI-eligible countries but middle-income countries desire to receive support. Implementing surveillance procedures in the former Soviet Union is difficult due to rigidity of health systems. There is a high proportion of prior antibiotic use and culture-negative CSF. PCR is important to increase the proportion of meningitis cases with a determined etiology. Surveillance data are limited in some areas, such as the timeliness of transport to the laboratory. Challenges include providing supplies to countries/sentinel sites is complicated; essential reagents are not available for local procurement; developing microbiological capacity; and ensuring appropriate culture media at sentinel sites. Training is ongoing with capacity building in the RRL and via the Health Protection Agency, UK. Pressures include to provide data on a short timeline, as a longer timeline is needed to build capacity given the complexity of IB-VPD surveillance. The proposed matrix
criteria/benchmarks are reasonable and broader context should be developed to guide decisions on which sites to maintain.

**IB-VPD Surveillance, EMR Overview** - H Ahmed

Tier 1 surveillance is conducted in 4 GAVI-eligible countries with a large number of sites. Additional surveillance systems are in place in non-GAVI countries including national laboratory-based surveillance and contribute important data. Low yield from cultures can be a problem and is likely due to use of antibiotics and inadequate culture laboratory media. Challenges include political upheaval and the security situation. The RO fosters MoH ownership of surveillance. Transportation and procurement of essential reagents to sentinel sites continues to be problematic, with the need to explore a better distribution system. Supervision is important; training and building capacity has been a focus and there is a need for continuous training. The question was posed whether national/sub-national production of high quality microbiological media be feasible given transportation costs to improve microbiology at sentinel sites. WHO RO support is essential for improving laboratory quality and providing data for network, but long-term sustainability will depend on building national capacity not just in laboratory but for procurement, importing supplies and exporting samples, etc.

**IB-VPD Surveillance, AMR/PAHO** - L Olivera & JM Gabastou

Pneumococcal conjugate vaccine has been introduced in 15 countries in AMR/PAHO with introduction accelerated in 2008. Meningitis surveillance is currently ongoing in a large number of countries, with pneumonia IBD surveillance also conducted in all countries except Brazil. Surveillance serves as a platform for special studies on vaccine impact. The current use of different vaccines or schedules provide opportunities to address specific questions around the optimization of vaccination schedules. SIREVA is a model network for laboratory surveillance for IBD but it does not provide population-based surveillance although it includes serotype distribution and antimicrobial resistance for nearly 40,000 isolates of Spn, Hi, and Nm over the past 10 years. This surveillance has demonstrated differences in Spn serogroup distribution within sub-regions and preliminary evidence shows changes in occurrence of common Spn serotypes following conjugate vaccine introduction. AM/PAHO has organized trainings and workshops twice yearly and there is regular communication within the network. The network includes published guidelines and standardized definitions, an essential list of supplies for laboratories, and annual publication of laboratory-based surveillance data. Visual aids (posters with case definitions and explanation of variables in reporting forms) have been placed in sentinel sites to improve data quality. Laboratory supervision includes external quality control.

**IB-VPD Surveillance, AFR Overview** - J Mwenda,

MoH ownership is of paramount importance to ensure high-quality surveillance and when selecting sentinel sites. Challenges and priorities in the surveillance network include ensuring use of standard case definitions, providing substantial investment in capacity building, and laboratory training. RRLs are centres of excellence that support the network. Laboratory supervision is important for trouble-shooting, and has demonstrated that some improvements can be made without additional resources but rather with better management of the existing laboratory resources.
On-site laboratory training is critical as is role of laboratory experts from RRLs. PCR is important to demonstrate the presence of important pathogens in culture-negative specimens. AFR is following up on the recent finding that in a few situations surveillance monies have remained in the WHO country office and not sent to MoH.

**General discussion points arising from Session:**
Recommendations from group discussions:

- Reduce the number of participating (and supported) sentinel sites for IBD surveillance to improve quality of the data. Data quality must be improved.
- Need to generate advocacy for this network and surveillance; need to improve the profile of the surveillance system to generate advocacy with decision makers at all levels.
- Need to more clearly state why we are conducting this surveillance and how this data will be used;
- Partnerships between MoH and academic centres (which often collect the best data but often do not submit data to WHO) is important to help overcome obstacles but is challenging.
- Involving NITAGS (National Immunization Technical Advisory Groups) may help improve surveillance and generate advocacy.
- With oversight by WHO and RO lab focal points, RRLs need to take a more proactive role in site visits and monitoring of sentinel site data and activities.
- MoH ownership is very important and must be strengthened.

**Improving Tier 1 IB-VPD Surveillance Quality**

Session: Wednesday, 14 September 2011

The structure of sentinel surveillance and the role of monitoring and supervision

**Session Objectives**

- Review the critical role of the MoH in monitoring and supervising sentinel surveillance, and explore potential strategies for such supervision
- Review experiences with successfully enhancing surveillance around introduction of the new meningitis vaccine in Burkina Faso, especially regarding strengthening the national surveillance system and the national laboratory’s role
- Explore potential partnerships to monitor and assess sentinel sites
- Conclude with potential decision of the priority and feasibility of monitoring and assessing sentinel sites at least twice yearly, and discuss potential mechanisms to do so, including utilizing surveillance partnerships with CDC and poliomyelitis

**Uganda MoH perspective: MoH role in managing and supervising surveillance and impact on surveillance quality** - IMwenyango

The Ugandan MoH presented the overall background of IB-VPD surveillance in Uganda. Surveillance for Paediatric Bacterial Meningitis was initiated in Mulago National Referral hospital in July 2001, and 3 more sentinel sites were added over the following years with support for expansion from netSPEAR and WHO. The MoH felt the expansion was necessary to develop a more representative epidemiology...
picture, and to build capacity in the hospital laboratories as consistent with IDSR goals. Two of the sentinel sites undertake RV surveillance.

The MoH is highly involved in surveillance activities and conducts advocacy in the form of sharing data with other ministries, supportive supervision visits, and conducts regular meetings with the involved partners. The data have been used to improve case management, and to increase GAVI support. Challenges for IB-VPD surveillance include widespread pre-hospital antibiotic use, limited human resources, the perception that surveillance is a special study, and the low motivation among healthcare workers which results in lack of adherence to SOPs. In order to improve surveillance quality, the MoH plans to share data more regularly with other Ministries in order to increase awareness of the system generally, conduct quarterly meetings with sentinel sites to problem solve as well as sensitize clinicians, and conducting train of the microbiology laboratory staff.

Burkina Faso: Lessons learned for IB-VPD surveillance - T Clark
The efforts to strengthen meningitis surveillance in Burkina Faso were presented in the context of MenAfriVac evaluation, and provided a historical overview of the activities in the country. Surveillance was strengthened by building strong partnerships and mentoring on all levels: laboratory, epidemiology, and data management. This surveillance has resulted in the collection of data that has demonstrated MenA impact. The guiding principles for this success included: 1) enhance local capacity infrastructure and expertise; 2) scale human resources appropriately to achieve the goal; 3) seek to build in sustainability; 4) demonstrate surveillance value locally to promote ownership; and 5) be disease agnostic. Critical factors for success of this work included the strong involvement of the MoH; in-country leadership; presence of local “champions”; and solving simple daily problems. The overall key was in good training, supervision, and monitoring that was conducted in “real-time” fashion and that local laboratory capacity was very high. The strong recommendation was put forward that surveillance efforts should seek to make good places better, and not train more places of lower capacity.

Potential partnerships: CDC Global Disease Detection - F Angulo
CDC’s Global Disease Detection (GDD) program was described in order to help WHO look for ways to harmonize with the IB-VPD network, in particular with Field Epidemiology Training Programmes, International Emerging Infections Programme, and laboratory strengthening. GDD works to strengthen global public health capacity within the context of International Health Regulations. GDD activities are based on the priorities of MoH. Potential partnerships between GDD and IB-VPD surveillance network might include monitoring of sites using a standardized tool.

The following recommendations were made:
- Supportive supervision, training, and problem solving as needs arise are key to ensuring high-quality surveillance.
- Continue sentinel site assessments and site visits. The capacity of microbiology laboratory staff should be regularly assessed and trainings held as needed.
- Share the data regularly within the country and with other Ministries in order to increase awareness of the system generally.
• **Conduct quarterly meetings** with sentinel sites to problem solve as well as sensitize clinicians, and

• **Partnerships** between MoH, academic centers (which often collect the best data but often do not submit data to WHO), and others such as the CDC Global Disease Detection colleagues are important to ensure high quality data, but these partnerships can be challenging. An initial step may be in combined efforts to monitor and assess sentinel sites, within the overall guidance of the MoH.

**Rationalizing Tier 1 meningitis sentinel site laboratory diagnostics**

Session: Wednesday, 14 September 2011

**Session Objectives**

• Review the experience of Bangladesh in conducting successful surveillance at sentinel sites and identify potential strategies applicable to other sentinel sites

• Review potential algorithms for sentinel sites laboratory diagnostic testing

• Review the critical role of PCR in diagnostic testing, including the potential addition of PCR testing for all CSF specimens

• Conclude with potential decisions of:
  - All sites to use the following tests on CSF: perform Gram Stain, then culture, then Binax (and/or LA if Hib vx not in the national programme)
  - All CSF specimens to be frozen and transported to RRL for PCR for identification of pathogens and Spn serotyping.

**Bangladesh: sentinel surveillance in a resource poor setting** - S Saha

An overview was provided of how sentinel surveillance is conducted in the context of a resource poor setting. In Bangladesh an algorithm for testing and specimen processing is used that depends on the volume of the available specimen. An important finding was that 86% of Spn positive specimens were culture negative, but were positive by other methods such as Binax or PCR. A critical aspect of surveillance is to work to promote buy-in from clinicians so that adequate specimens are collected. Timely reports to clinicians are critical to increase their involvement.

**The role of PCR: lessons learned from AFR and The Gambia RRL** - S Jarju

The structure, testing algorithm, and preliminary data from the Gambia RRL activities were presented, and included the distribution of Spn serotypes by country, age, and season. Culture-negative CSF specimens tested by PCR detected an additional 26% of meningitis cases (compare to 4% by culture alone). Later, much discussion followed about the importance of providing numbers and denominators when presenting data otherwise the presentation can be quite misleading. *(Dr. Claire Broome gave an ad-hoc presentation demonstrating the need to use appropriate numerators and denominators to ensure consistent data interpretation.)*

**Proposed algorithm for sentinel site diagnostic testing** - M Slack

WHO and the WHO GRLs have been working to develop a standardize algorithm for sentinel site laboratory CSF diagnostic testing. The draft testing algorithm for Tier 1 meningitis specimen (CSF) processing and testing was presented to receive inputs which will be considered in the revision of the algorithm. Key discussion points included which tests should be prioritized, including the pros and cons of the
existing rapid tests, and in which order the tests should be performed. Recommendations include:

- CSF should arrive to the laboratory within 1h after collection
- Culture the CSF asap, too much manipulation increases contamination risk
- It is not needed to add a MacConkey plate to the primary media
- The CSF aliquot for PCR must not be used for any other testing, including Binax.
- Add a rapid diagnostic test to increase the diagnostic yield
- Binax should not be used on the supernatant as recommended by the manufacturer
- Specify that Real time-PCR is the PCR to be used for the identification of the three organisms

**Improving RRL support: roles and responsibilities of RRLs in supporting sentinel and national laboratories**

**Session Objectives**

- Review the current roles and responsibilities of each level of laboratory in the network (sentinel, national, regional, and global)
- Determine the current needs, including training, of RRLs in order to fulfill the stated roles & responsibilities and whether these needs are being met

**RRLs: Global Viewpoint** - F Serhan

The 2010 roles and responsibilities of the RRLs were summarized as well as the results from a survey of the RRLs to assess their performance in terms of those roles/responsibilities. In brief, the roles and responsibilities of the RRLs were emphasized to be: increasing the capacity of the national laboratories (NLs) and sentinel site laboratories (SSLs) by assisting WHO and MoH with site visits and assessments; performing validation on a certain percentage of the SSLs and NLs results; and participating in the EQA program. Overall, the RRLs were encouraged to do site visits and provide training to the countries in their respective regions.

**Regional viewpoints:**

**AFR:** Three RRLs (MRC the Gambia, NICD in South Africa, and Kilifi in Kenya) have been identified. The MRC Gambia laboratory serves 20 sentinel sites, and accomplishments from the past year included: participating in the EQA program; hosting two training workshops for members of the network; visiting 7 sentinel site labs for on-site training; providing guidance/reagents to the NLs and sentinel site labs; contributing to WHO meetings; and conducting research of the effect of PCV on Spn sequence types in the region. NICD in South Africa serves 5 sentinel sites, and accomplishments for the past year included: hosting training in West, East, and South Africa; visiting 1 sentinel site providing guidance/reagents to laboratories in the region; and coordinating the EQA program for the IB-VPD network. The Kilifi laboratory in Kenya is transitioning from netSPEAR to the WHO IB-VPD network; despite challenges faced by this transition, the Kilifi laboratory participated in the EQA program, performed duplicate testing, and performed serogrouping and serotyping. The Kilifi laboratory does not have the personnel to fully support the sites and do site visits; and there are no strong NLs in the area. To remediate these
personnel issues, the Kilifi laboratory would need to hire someone to fully support the sites, but the laboratory noted that it is hard to recruit someone for that type of position with only a 1 year contract which is the length of funding offered by WHO.

**AMR**: Did not present.

**EMR**: The RRL (Central Public Health Laboratory, Ministry of Health, Egypt) summarized their major accomplishments from the past year that included passing the EQA with 100% proficiency; performing confirmatory specimen testing two times for Afghanistan, Pakistan, Syria, and Egypt; did some on-site training in the Sudan; and provided guidance and TI media for all of the countries in the region.

**EUR**: The RRL (Gabricevsky Research Institute for Epidemiology and Microbiology, Moscow, Russia) summarized their main activities which included bacteriological, serological, and molecular genetic testing in support of 2 countries in the IB-VD network, training at the RRL and in country, and visits to 3 sentinel sites.

**SEAR**: The RRL (CMC, Vellore, India) did not conduct any visits or assessments at sentinel sites. Some Spn serotype data was presented. There has been an effort to change the primer combination of the multiplex PCR serotyping assay for Spn to tailor it for the region.

**WPR**: RRL activities have not yet commenced. IBD training workshop held in March/April 2011, but RRL support to their NLs and SSLs has not begun.

**Discussions**

There was some discussion and expression of concern about the availability of global SOPs/guidelines and how much standardization should be achieved in terms of protocols in the network. SOPs for training and testing are still in development, regional SOPs will need to be developed after receipt of global SOPs. SOPs are also needed for tests and primers, etc. The distribution of the global Meningitis laboratory manual will be undertaken during 2011, which will be an important contribution to the network. The soon to be released laboratory manual was quite lengthy, and that a simpler and more user friendly version would be useful for sentinel sites. The planned laboratory poster that is being developed in concert with the laboratory manual may help to fill this need.

WHO ROs have been working with RRLs to identify which countries will require support and to best target support. In general, the WHO RO designates which laboratories function as NLs and sentinel labs, identifies weaknesses, and puts together a team to visit a site to correct those identified weaknesses. Trainings can also be organized.

Questions were raised that included: 1) From where will the laboratories receive primers/probes? 2) Can WHO cement which diagnostic tests will be used in the network going forward? 3) When will the meningitis manual be ready? 4) Are all laboratories in the network using the same methodologies?
Overall, the discussion highlighted the following topics: 1) Expression of concern by the RRLs about sustainability/feasibility of the network, about wanting to be in a partnership that has a public health impact; 2) The roles of the RRLs are still amorphous, and this ambiguity makes it difficult to make decisions/set priorities for training, site visits, etc; and 3) The funding structure of the network hinders commitment to the project, i.e., it is hard to keep people motivated and make personnel decisions when there is no more than a 1 year funding commitment for the network.

Agreed next steps
- RRLs play a vital role in the network, and are agreeable to continuing to work with WHO in support of the IB-VPD network, which is an important public health global initiative.
- RRLs urged WHO to develop a more sustained funding stream, as the current one-year funding allocations prohibit the recruitment of staff and limit long-term planning.
- The draft laboratory manual for meningitis should be released as soon as feasible, along with the accompanying laboratory poster.
- The roles and responsibilities of the RRLs should be revisited, in order to provide further clarity in this regards.

Session  Laboratory external quality assurance and quality control

Session Objectives
- Present the results of 2011 EQA, challenges and lessons learned
- Plan for next steps to involve all the laboratories in the network in the EQA
- Present a strategy plan for the QC implementation
- Plan for next steps to implement the QC in all the laboratories of the network
- Conclude with potential decisions:
  - Twice yearly EQA for all laboratories in the network
  - Once yearly QC for all laboratories in the network
  - Development of standard criteria to judge performance quality and actions for poor performing laboratories

Global EQA Experience - L de Gouveia
South Africa’s EQA department’s standard evaluation was used for public and private laboratories in the country as well as and laboratories throughout Africa for a number of organisms. WHO requested expanding the existing EQA for meningitis organisms in order to establish a standardized global EQA for the IB-VPD network. This EQA was launched in 2011, with specimens sent out with surveys for the laboratories. Laboratories are evaluated in 5 areas (microscopy, culture and identification, serotyping, antimicrobial agents selection for testing and antimicrobial susceptibility). Results of two EQA surveys conducted during 2011 were presented: out of 121 potential participants, 39 laboratories received the proficiency testing (PT) panels in the first survey and 57 laboratories in the second. Internal quality control,
poor quality media, difficulty with basic tests, and correlating gram stain with culture results were identified as common problems. Difficulties included identification and serotyping of Hi, serogrouping of Nm. Lessons learned include that shipping and importation to some WHO regions is cumbersome and time consuming, logistical issues should be sorted out with each RO before the PT shipment. Thus, sending of samples on Trans-isolate (TI) media should be reconsidered and focus should be given on lyophilized samples. Additionally, include a laboratory questionnaire to assess the participant laboratory capacities and add PCR to the areas of evaluation for the reference laboratories. Carla Talarico’s talk on QC implementation was not given due to lack of time.

Next Steps and Agreements:
1) The global IB-VPD EQA is an important component of the surveillance network, and should be continued on an annual basis.
2) The contact information used to report results back to laboratory should be regularly updated and should include the WHO regional laboratory coordinator;
3) Feedbacks on results should be provided as soon as possible to the individual laboratories and WHO, so that the laboratories and WHO can begin to plan appropriate follow up.
4) A global QC programme will not be launched at this stage, as it would be duplicative of Regional QC practices
5) A smaller technical laboratory working group should be convened to develop a standardized protocol of activities to be undertaken for laboratories that do not pass the EQA.

III f. Ad hoc technical advisory group closed session: next steps to improve IB-VPD surveillance

The ad-hoc group met following the surveillance meeting and noted that:
• Rotavirus surveillance network was functioning to a high degree, and producing important data for national decision making.
• WHO should focus on improving IB-VPD Tier 1 meningitis surveillance during the coming year.
• WHO should develop basic eligibility criteria for IB-VPD Tier 1 sites, and should provide support for as many sites as can meet those criteria.
  o Furthermore, WHO should then focus on a few selected sites to improve their performance capacity. This needs to be a transparent process.
• The purpose of the surveillance should be clearly articulated. In this regards, points should be included that the data is useful to Ministers to justify their budget requests for vaccine procurement and the capacity building component of surveillance
• More emphasis should be placed on engaging clinicians for IB-VPD surveillance.
### Agenda: Sunday, 11 September  
**12:00 - 17:00  Closed Session for WHO Participants Only**

### Agenda: Monday, 12 September  
**Focus Issue: Rotavirus Laboratory Network**

<table>
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<th>Chair: C Mantel</th>
<th>Rapporteur: A Wasley</th>
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<tr>
<td><strong>Time</strong></td>
<td><strong>Session 1: Opening, Status of the Network, and EQA/QC Issues</strong></td>
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| 08:30-09:00     | Welcome and goals of meeting  
Update on the global rotavirus surveillance network, funding, and  
the status of the rotavirus laboratory network | C Mantel  
M Agocs/F Serhan, HQ |
| 09:00-10:30     | Status of rotavirus surveillance in the WHO Regions  
• HQ, AFR and AMR/PAHO updates  
Discussion  
• EMR and EUR updates  
Discussion | J Mwenda, AFRO  
L Olivera, AMR/PAHO  
H Ahmed, EMRO  
D Videbak, EURO |
| 10:30-11:00     | **Coffee Break** (Note: Parallel Session on Data Management Follows Coffee Break) |
| 11:00-12:00     | • SEAR and WPR updates  
Discussion | P O’Connor, SEARO  
K Fox & F Paladin, WPRO |
| 12:00-13:00     | Rotavirus laboratory EQA and QC:  
• Global EQA experience, QC draft protocol and next steps  
Discussion and next steps | M Bowen, GRL |
| 13:00-14:00     | **Lunch** |
| **Chair: M Bowen** | **Session 2: Standardizing Procedures and Supplies** | **Rapporteur: F Paladin** |
| 14:00-16:00     | Rotavirus laboratory: Developing standard operating procedures,  
including for strain characterization, and standardizing supplies  
• Summary of RRL responses to standard questionnaire  
• RRL inputs: AFR, AMR/PAHO, EMR, EUR, SEAR, WPR  
Discussion | R Gautam  
RRLs: AFR, AMR/PAH  
EMR, EUR, SEAR, WP |
| 16:00-16:30     | **Coffee Break** |
| 16:30-17:00     | Discussion continued |
| **Chair: J Gentsch** | **Session 3: Summary of Meeting** | **Rapporteur: F Paladin** |
| 17:00-17:30     | Summary of meeting outcomes and action items  
Discussion | M Bowen,  
F Serhan, M Agocs |
Monday: WHO Data Management Session
Defining Surveillance Data Management Issues and
Next Steps Forward to Streamline the System

CCV, Salle C: Geneva, Switzerland

Chair: M Gacic-Dobo  Rapporteur: L Dumolard

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<td>L Dumolard</td>
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<td>11:30-13:00</td>
<td>Regional Office data management situational updates</td>
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<td>• Existing data management system</td>
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<td>• Who provides data to the RO?</td>
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<td>• How often is data provided?</td>
<td>AMR</td>
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<td>• What is the data management software?</td>
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<td>• How often does the RO analyse the data?</td>
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<td>• How is the data used?</td>
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<td>• How many data management staff are there currently?</td>
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<td>• How are data reported back to the sentinel site?</td>
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<td>• Identified strengths of the system</td>
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<td>• Recommendations to improve the system</td>
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<td>Discussion</td>
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<td>13:00-14:00</td>
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<td>14:00-16:00</td>
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<td>HQ situational update</td>
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<td>IB-VPD surveillance and case based data: The possibility of linking data from Regional Reference Laboratories with clinical data from the case</td>
<td>All participants</td>
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<td>Discussion and problem solving</td>
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<td>16:00-16:30</td>
<td>Coffee Break</td>
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<tr>
<td>16:30-17:00</td>
<td>Review of action items from meeting</td>
<td>L Dumolard</td>
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### Agenda: Tuesday, 13 September

**Focus Issues:** Global Update, Using Surveillance Data, and Improving IB-VPD Data Quality

**Chairs:** JM Okwo-Bele & T Cherian  
**Rapporteur:** S Schwartz

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<td>Welcome and goals of meeting</td>
<td>JM Okwo-Bele</td>
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<tr>
<td>09:00-10:00</td>
<td>Update on global rotavirus (RV) and invasive bacterial vaccine preventable disease (IB-VPD) surveillance networks</td>
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<td>• Status of introduction of new vaccines</td>
<td>C Mantel</td>
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<td>• New vaccines surveillance for RV and IB-VPD: Implementation of action items identified during 2010 surveillance meeting, status, and funding</td>
<td>M Agócs</td>
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<td>• Status of the global RV and IB-VPD laboratory networks</td>
<td>F Serhan</td>
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<td>Discussion</td>
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**Coffee Break**

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<tr>
<th>Time</th>
<th>Session 6: Status of IB-VPD surveillance and potential actions to improve quality of Tier 1 meningitis surveillance</th>
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<td>10:00-10:30</td>
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<td>10:30-12:15</td>
<td>Rotavirus surveillance: using data to inform vaccine policy</td>
<td>Co-Chair: U Parashar</td>
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<td>• Introductory comments and overview</td>
<td>U Parashar</td>
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<td>• Paraguay: establishing rotavirus surveillance and using data to make decisions regarding vaccine introduction</td>
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<td>• Sudan: decision making &amp; measuring impact</td>
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<td></td>
<td>• Americas Region: Assessing rotavirus vaccine impact</td>
<td>L Oliveira</td>
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<td>• Using rotavirus data to optimize vaccination schedules</td>
<td>C Sanderson</td>
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<td>• Opportunities to share and disseminating information</td>
<td>U Parashar</td>
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<td></td>
<td>Discussion</td>
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**Session 6 Continued**

<table>
<thead>
<tr>
<th>Time</th>
<th>IB-VPD surveillance status in the WHO Regions, continued</th>
<th>Rapporteur</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:15 - 12:30</td>
<td>Summary of proposed recommended activities to improve Tier 1 IB-VPD surveillance data quality during 2012</td>
<td>M Agócs</td>
</tr>
<tr>
<td>12:30-13:00</td>
<td>WPR update with views on matrix and discussion</td>
<td>K Fox/ F Paladin</td>
</tr>
<tr>
<td>13:00-14:00</td>
<td><strong>Lunch</strong></td>
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**Session 6 Continued**

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<tbody>
<tr>
<td>14:00-15:30</td>
<td>SEAR update with views on matrix and discussion</td>
<td>P O’CONNER</td>
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<td>EUR update with views on matrix and discussion</td>
<td>AM WASLEY</td>
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<td>EMR update with views on matrix and discussion</td>
<td>H AHMED</td>
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<tr>
<td>15:30-16:00</td>
<td><strong>Coffee Break</strong></td>
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<tbody>
<tr>
<td>16:00-17:30</td>
<td>AMR/PAHO with views on matrix update and discussion</td>
<td>L OLIVERA &amp; JM GABASTOU</td>
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<td>AFR update with views on matrix and discussion</td>
<td>J MWENDA</td>
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<tr>
<td>18:00-20:00</td>
<td><strong>Reception - CCV</strong></td>
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# Agenda: Wednesday, 14 September

## Focus Issue: Improving Tier 1 Meningitis IB VPD Surveillance

### Chair: Samir Saha  
Rapporteur: S Schwartz

<table>
<thead>
<tr>
<th>Time</th>
<th>Session 7: Improving Tier 1 IB-VPD surveillance quality</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>08:30-10:00</td>
<td>The structure of sentinel surveillance: role of monitoring, supervision, and training</td>
<td>I Mwenyango</td>
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<td>• Uganda Ministry of Health (MoH) perspective: MoH role in managing and supervising surveillance, and impact on surveillance quality</td>
<td>T CLARK</td>
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<td>• Burkina Faso: Lessons learned for IB-VPD sentinel surveillance</td>
<td>F ANGULO</td>
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<td>• Potential partnerships: CDC GDD</td>
<td>M Agocs</td>
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<td>• The polio partnership and WHO clinical and laboratory assessment tools</td>
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<td>Discussion</td>
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<td><strong>Potential recommendation:</strong> priority Tier 1 IB-VPD sentinel sites to be assessed via standard tool by MoH, WHO, or partners with RRLs 2x per year</td>
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<tr>
<td>10:00-11:00</td>
<td>Rationalizing Tier 1 meningitis sentinel site laboratory diagnostics</td>
<td>S SAHA</td>
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<td>• Bangladesh: structure of sentinel surveillance in a resource poor setting</td>
<td>S JARU</td>
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<td>• The role of PCR: lessons learned from AFR &amp; The Gambia RRL</td>
<td>M Slack</td>
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<td>• Proposed algorithm for sentinel site diagnostic testing</td>
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<td><strong>Potential recommendation:</strong> all sites perform Gram Stain then culture then Binax (and/or LA if Hib vx not in national programme) and freeze all CSF for transport to RRL for PCR</td>
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<tr>
<td>11:00-11:30</td>
<td><strong>Coffee Break</strong></td>
<td>Rapporteur: C Talarico</td>
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<tr>
<td>11:30-13:00</td>
<td>Improving RRL support Roles and responsibilities of RRLs in supporting sentinel and national labs</td>
<td>F Serhan</td>
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<td>• RRL viewpoint: status and needs to fulfil roles and responsibilities</td>
<td>RRLs: WPR, SEAR, EUR, EMR, AMR/PAHO, AFR</td>
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<td>Discussion: identification of needs and gaps</td>
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<td><strong>Potential recommendation:</strong> RRLs with, WHO &amp; MoH oversight, directly assess and support sentinel laboratories, in collaboration with national laboratories as appropriate</td>
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<td>13:00-14:00</td>
<td><strong>Lunch</strong></td>
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### Chair: T Cherian

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<tr>
<th>Time</th>
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<tbody>
<tr>
<td>15:00-16:00</td>
<td>Laboratory external quality assurance and quality control:</td>
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<td>Rapporteur: B Flannery</td>
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<td>• Global EQA experience, plan for QC and next steps</td>
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<td></td>
<td>• Plan for QC and next steps</td>
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<td>Discussion</td>
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<td><strong>Potential recommendations:</strong> 1) 2x yearly EQA for all labs; 2) 1x yearly QC for all labs; 2) development of standard criteria to judge performance quality and actions for poor performing laboratories</td>
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<tr>
<td>15:30-16:00</td>
<td><strong>Coffee Break</strong></td>
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<tr>
<td>16:00-17:00</td>
<td>Discussion on matrix &amp; meeting wrap-up</td>
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<td>T Cherian</td>
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<tr>
<td>17:00-18:30</td>
<td><strong>Closed session in Salle C</strong></td>
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<td>C Van Beneden: Overall meeting rapporteur</td>
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