MEETING REPORT

Global Rotavirus and Pediatric Diarrheal Surveillance Network Meeting

19-20 November 2019

JW Marriott Hotel
Rio de Janeiro, Brazil
Meeting Report: Global Rotavirus and Pediatric Diarrheal Surveillance Network Meeting
Tuesday and Wednesday, 19-20 November 2019
JW Marriott Hotel, Rio de Janeiro, Brazil

Meeting Objectives
- Review data from Global Rotavirus (10 years) and Pediatric Diarrhea (2 years) Surveillance Networks
- Discuss priorities and future activities for rotavirus and pediatric diarrhea surveillance

Day 1, Session I: Global Rotavirus and Pediatric Diarrhea Surveillance Updates
Presenters: Adam L. Cohen and Fatima Serhan, WHO HQ

Presentation overview
The first two years of prospectively enrolled Global Pediatric Diarrhea Surveillance from 33 surveillance sites in 28 countries was presented. While there is a clear impact of rotavirus vaccine at country, regional, and global level, rotavirus remains leading cause of severe diarrhea in children <5 year of age in all regions. Norovirus, Shigella, and adenovirus are next most common, though norovirus causes fewer deaths than the other two. ETEC is the 8th most common cause of severe diarrhea and the 6th most common cause of diarrhea deaths. Optimised rotavirus genotyping methods across the network have generated invaluable, globally representative rotavirus genotype data. Ongoing surveillance for rotavirus and pediatric diarrhea critical to continue rotavirus vaccine impact evaluations, including for new rotavirus vaccines, and to generate burden data and evaluation platforms for pipeline vaccines such as for Shigella, norovirus, and ETEC.

Discussion and Action Points
- Vaccine coverage is an important consideration when evaluating vaccine effectiveness.
- May expect a high rotavirus burden even after vaccine introduction since vaccine effectiveness is only around 50% and varies in different settings.
- Many countries in AFRO had a rotavirus spike in 2017; may want to investigate this further.
- Assess if there are other factors, such as quality of surveillance, that could be associated with changes in etiologies seen in the network.
- Low rates of Shigella in WPRO are surprising given estimates from other sources. Need to follow-up with sites to understand the disease epidemiology and healthcare patterns to assess whether the low rates of Shigella are due to the way the surveillance is conducted.
- Are the network’s adenovirus estimates reliable? May be over-ascribing deaths to adenovirus due to limitations in applying severe diarrhea and mortality profiles when weighting.

Day 1, Session II: Performance and support: Surveillance sites

Monitoring and Evaluating the Performance of GPDS Participating Sites
Presenter: Tomoka Nakamura, WHO HQ

Presentation overview
From the start of GPDS in 2017, each participating sentinel site is monitored by evaluating the number of stool samples tested by TAC Array Cards per quarter and per year. A sentinel site was evaluated as
having high performance criteria if it followed the GPDS protocol, which is to have 25 stool specimens tested by TAC per quarter and to report surveillance data for 12 continuous months per year. The minimum performance criteria are having at least 20 stool specimens tested by TAC per quarter and at least 10 months of surveillance data reported per year. For the sentinel sites that did not meet either of these criteria, evaluating the pattern of surveillance throughout the year is critical. Identifying the reasons for not being able to fully meet the GPDS protocol (e.g. low sample volume, halt in conducting surveillance) is also key to resolve issues as soon as possible.

The clinical presentation of the stools collected for GRSN and GPDS was evaluated to assess the overall distribution of the types of diarrhea presented in each country (acute watery, acute bloody, persistent water, and persistent bloody). This demonstrated whether the sentinel site participating in GPDS has successfully expanded their enrollment criteria to include bloody diarrhea cases.

A new site assessment tool was developed last year to evaluate the performance of sentinel sites participating in GPDS. This tool was revised this year by incorporating several components of the GRSN assessment tool, including sections on the method of case detection and reporting, specimen collection and timeliness, and data management and confidentiality. The assessment of malnutrition through GPDS is an optional component of the tool.

Experience using site assessment tool in Fiji  
*Presenter: Nyambat Batmunkh, WHO WPRO*

**Presentation overview**

The GPDS site assessment tool was piloted at Colonial War Memorial Hospital in Fiji. Assessment using the tool identified considerations such as conducting retrospective chart review (when real-time is preferred) and samples waiting multiple days before transport. Action points of implementing regular refresher trainings at the hospital level for incoming staff and identifying a staff member to have responsibility for sample collection and shipment were developed based on the site assessment. Additionally, the site assessment revealed that there was no staff responsible for data entry and transmission, explaining why data had not been transmitted to the Regional Office since Q2 of 2018. Overall the tool was successfully used to identify potential issues at the Fiji site, and suggestions for improvements to the tool were sent to WHO HQ.

**Discussion and Action Points**

- Site assessment should consider prior lessons learned (such as issues with linking data) and be tailored to address those known issues.
- It is critical to continue an evaluation of all participating GPDS sites including evaluating the number of stool samples tested by TAC and the characteristics of diarrhea detected by surveillance throughout the year.
- The site assessment tool will be shared to all Regional Offices and any countries that are interested in utilizing it to evaluate their GPDS site. The tool can be translated to the country’s main language. WHO HQ is receptive to feedback on the tool.
- The laboratory assessment tool established for GRSN can be potentially expanded to include an evaluation for TAC Array testing at the Regional Reference Laboratories (RRLs).
Country vaccine impact studies: CDC perspective

Presenter: Jackie Tate, U.S. Centers for Disease Control and Prevention

Presentation overview
As of 2017, over 60 countries had past or on-going rotavirus vaccine impact or effectiveness evaluations; these showed reductions in all-cause diarrhea hospitalizations and mortality following rotavirus vaccine introduction. The vaccine provides good protection against many circulating strains but has been shown to be more effective in countries with lower child mortality and against more severe disease. Countries interested in evaluating the impact of rotavirus vaccine can use surveillance platforms. Countries can also determine vaccine effectiveness with a case-control study design evaluating the odds of vaccination among cases compared with controls. Current data on vaccine impact studies can be found in recent journal supplements in *Clinical Infectious Diseases* and *Vaccine*. Anticipated data in the next several years includes impact and effectiveness studies of new Indian-manufactured vaccines and studies of impact and effectiveness of Rotarix in regions with previously limited data.

Discussion and Action Points
- There is no conflict of a site doing both GPDS and a vaccine effectiveness study, but there was confusion in a site where GPDS and a vaccine effectiveness study were rolled out at the same time.
- U.S. CDC can provide tools and evaluations to help countries develop good study designs for vaccine impact studies.
- There is data from high income countries showing herd immunity from rotavirus vaccine, but herd immunity has not been adequately looked at in low-and-middle-income countries yet.
- There may be some rotavirus picked up from ELISA due to vaccine shedding in the stool, however this should not be enough to obscure the impact of vaccination on rotavirus prevalence.

Group discussion: How can WHO support sites to maintain/strengthen surveillance network? What other activities need to be coordinated with the network?
- Regional meetings between regional office and countries/sites and site visits to assess surveillance methods are extremely important, but there is a lack of resources for this support.
- Turnover of staff at country/site level leads to a constant need for new trainings and can result in unfilled positions which significantly affects the ability to perform surveillance.
- Important for WHO HQ to provide GPDS country analyses in editable format so they can be translated as needed.
- Sites for GPDS were initially chosen due to good performance; however, performance of the sites has changed over time. Need to discuss if there are sites that should be removed or added to the GPDS network and how to do that.
- Need a procedure for helping countries transition to supporting surveillance on their own to ensure sustainability of the surveillance.
- Need to think about how to better advocate for and show the value of the surveillance network; potential to use the network as an example of a comprehensive VPD surveillance program.

Day 1, Session III: Performance and support: Laboratory

Improving the quality of Global VPD sentinel surveillance data
Presenter: Sébastien Antoni, WHO HQ

Presentation overview
The WHO Immunization Information System (WIISE) will be released in the coming months to facilitate the management, analysis and dissemination of immunization and VPD surveillance data across all levels of WHO. It is expected that rotavirus and pediatric diarrhea surveillance data will migrate to WIISE in 2020. A generic, non-disease specific data management pamphlet for VPD surveillance was finalized. It will provide guidance to data managers working on VPD surveillance at different levels. The document will be submitted for internal clearance soon. Figures were presented highlighting the increasing quality of GPDS data from 2017 to 2018. Some areas still require attention such as the collection of diarrhea duration. The difficulty in linking surveillance data with TAC results in some countries was highlighted. Recommendations were to include information on country/year as part of the case ID (at site level) or in the experiment name (at RRL level) and to share the lists of cases randomized (at RO level) so that these lists can be cross-checked by the RRL before testing and HQ when linking data.

Discussion and Action Points
- Concern about bottlenecks at WHO HQ with WIISE system. May need to include tasks at the regional level.
- Cleaning of data should be an on-going process instead of waiting until receiving the list of TAC samples selected to be tested.

Quality assurance systems: Digging Deeper into Laboratory Results from GPDS
Presenter: Tomoka Nakamura, WHO HQ

Presentation overview
Implementing a quality assurance system is crucial when the RRLs test the stool samples for GPDS. It is particularly important to evaluate the quality at an early stage such as when the RRLs receive the sample shipment, and includes checking the temperature, volume of each sample, status of the sample tube, and whether the unique ID matches with what is provided in the surveillance database. These qualities are important to document for quality control. A lab swipe test is encouraged to detect any potential contaminations within the laboratory. During the nucleic acid extraction stage, a “blank” should always be included for later quality assessment (i.e. one per extraction set). The extracted samples and blanks are spiked with controls and when they are run on PCR using the TAC Array cards, these internal controls should be detected. Finally, the unique ID number should be verified for each sample before uploading all the TAC data onto MuSIC, so these results can be linked with their surveillance data. This year, a data external quality assessment (EQA) pilot was implemented of which six RRLs participated. Three “raw” TAC files (i.e. PCR amplification curves) were analyzed and the evaluation was both quantitative and qualitative. Overall, the RRLs performed well on this pilot exercise. Additionally, the majority of the RRLs appeared to have less contamination among their labs in 2018 compared to 2017.

As part of GRSN, laboratories have continued to participate in the rotavirus EQA exercise. In 2018, 98% of the 107 participating laboratories passed the EIA component while 95% of the 57 participating laboratories passed the genotyping component. There will not be a 2019 EQA rotavirus exercise but new EQA panels are planned to be distributed during the first quarter of 2020.

Discussion and Action Points
• Quality assurance activities must be sustained for rotavirus including external quality control for confirmatory testing implemented in national, regional and global laboratories (e.g. sharing of specimens). Quality assurance also includes continuing the rotavirus EQA exercise.
• Quality management systems must be reinforced at the RRLs for TAC testing. It is challenging to enhance TAC quality assurance systems because of the necessity to test multiple pathogens and the limited supply and high cost of TAC cards and reagents to implement an EQA exercise.
• Data EQA exercise is one way to reinforce the quality management system for TAC testing and it is available for any RRL that is interested.
• Concern has been raised about randomization of TAC samples only once per year due to potential of delaying results and burden placed on RRLs.
• Poor performance at sentinel sites may be due to turnover in staff, equipment shortages, use of old protocol, etc., so site visits are very important to understand where the issue is.

Rotavirus EIA compared with Rotavirus TAC
Presenter: James Platts-Mills, University of Virginia

Presentation overview
PCR detection without a quantitative cutoff or attribution modeling should be interpreted with caution since there is PCR detection at low-levels of rotavirus not thought to be attributable to disease. While PCR is more sensitive than EIA, the EIA prevalence and PCR attributable fraction provide similar estimates. There are several sites with a higher number of PCR-attributable/EIA-negative cases, and there appears to be a difference in vaccine impact based on whether PCR or EIA is used, namely that there is a greater reduction in proportion positive with EIA compared to PCR. Using clinical characteristics and the presence of other pathogens, these PCR-positive/EIA-negative discordant cases appear to be consistent with rotavirus diarrhea.

Discussion and Action Points
• AFRO labs sometimes retest PCR+/EIA- samples, so maybe we could analyze those retests.
• Potential for picking up children shedding vaccine. Could stratify analysis by age-eligibility for vaccine or look at vaccine history if available.
• Could retest or dilute samples before running EIA if there is a possibility that antigen is clumping.

Day 1, Session IV: Performance and support: Regional and global experience

Surveillance experience from PAHO
Presenter: Lúcia de Oliveira and Gloria Rey, WHO PAHO

Presentation overview
PAHO was the first region to introduce rotavirus vaccine globally and has data showing a clear decrease in rotavirus disease after vaccine introduction. There are now 6 sites participating in GPDS in the PAHO region with the addition of Bolivia in 2018. Completeness of the ten critical variables collected in the case-based surveillance data (especially Stool_ID, Bloody_YN, and Stool_collected) varies by site. Data collection and management are noted areas of improvement. Another noted area of improvement is ensuring adequate numbers of GPDS samples are selected and sent to RRL for Taqman Array Card (TAC)
testing. The results of GPDS show rotavirus, norovirus, Shigella, and adenovirus to be leading etiologies for pediatric diarrhea in the PAHO region. However, the leading pathogen varies by country. Rotavirus is the leading cause of pediatric diarrhea in Nicaragua, Bolivia, and Peru; Shigella is the leading cause of pediatric diarrhea in Honduras and Paraguay; and norovirus is the leading cause of pediatric diarrhea in Ecuador.

SEAR perspective on two new rotavirus vaccines in India

Presenter: Emmanuel Tondo, WHO SEARO

Presentation overview

Production of two new, WHO pre-qualified rotavirus vaccines in India has enabled vaccine procurement for more than half of SEAR’s annual birth cohort and is an opportunity for other countries. The rotavirus vaccine introduction was a phased introduction and financed by the Government of India (except for in one state which had Gavi support). The rotavirus vaccines are considered interchangeable under the routine immunization program, and both vaccines have been shown to be safe to use. As of May 2019, only 3 cases intussusception have been recorded (with no deaths) out of 50 million doses administered (i.e. 1 case/5.5 million rotavirus vaccine administrations. The success of India’s rotavirus vaccine introduction was due to wide dissemination of training video, hands-on training, extensive supervision of trainings, and intensive field monitoring and handholding.

Discussion and Action Points

• While surveillance data shows early impact of the new rotavirus vaccines in India, other countries and regions are hesitant to introduce without data from their country or region. Vaccine impact studies may be encouraged in other regions besides SEARO.
• WHO is currently in the process of updating the position paper for rotavirus vaccines to include information about the two new vaccines and provide guidance about interchangeability of the vaccines.
• Ongoing studies are looking at vaccine safety.

Advancing enteric vaccines and full value of vaccines assessment (FVVA)

Presenter: Ibrahim Khalil, WHO HQ and University of Washington

Presentation overview

Achieving vaccine impact goes beyond just determining the quickest pathway to licensure. It is important to consider data requirements for vaccine candidates up front. For example, burden of disease to inform demand estimates, data needs for policy recommendations, and data needed for LMICs to uptake vaccine should all be considered. The Full Value of Vaccines Assessment (FVVA) is a concept in development that will provide a resource to advocate for the development of vaccines, inform investment decisions, and accelerate suitability for and accessibility of vaccines to LMICs. Specifically, for diarrheal disease, the FVVA considers the importance of surveillance in informing disease burden estimates, monitoring strain diversity, and monitoring changes in burden and strains over time. It also seeks to move beyond using just mortality to measure diarrheal disease burden and to also quantify morbidity and long-term sequelae.

Discussion and Action Points

• This work is extremely important because there is always a need to convince donors to fund vaccine development.
• The network should consider how to advocate for the full value of surveillance and how that can fit into the full value of vaccine assessment.

**Day 2, Session I: Laboratory technical considerations**

**Rotavirus TAC genotyping validation**  
*Presenter: Matthew Esona, U.S. Centers for Disease Control and Prevention*

**Presentation overview**  
The Rotavirus Surveillance and Molecular Epidemiology Team at the U.S. Centers for Disease Control and Prevention (CDC) have been collaborating with the team at University of Virginia (UVA) to validate the rotavirus genotyping assays to be included on the new TAC card. They propose adding 20 qRT-PCR assays on the new TAC card to detect rotavirus strains, genotype VP7 and VP4 genes, and Rotarix® and RotaTeq® strains. To develop the assays, consensus sequences for genotypes were determined and primers and probes were designed. Known rotavirus positive and rotavirus negative samples of varying genotypes were used to test and select probes. Next steps are to optimize G1, G9, and P[14] assays which showed low sensitivity, and to provide probe sequences for synthesis by ThermoFisher and CDC primer/probe mixes to UVA in order for Taqman array cards to be created and shipped to labs for testing of 2019 TAC samples.

**Composition of new GDPS TAC card layout**  
*Presenter: Darwin Operario, University of Virginia*

**Presentation overview**  
A new TAC card will be introduced for the testing of 2019 TAC samples and moving forward. Figures of 2 previous versions of TAC array cards were presented. The card will be designed to identify a broad range of infectious diarrhea etiologies, subtypes of priority pathogens such as rotavirus and Shigella, and, with space available, antimicrobial resistance. Reasons targets were proposed for removal include low detection in 2017 and 2018, no evidence of providing useful information, or duplication with other targets on the card.

**Discussion and Action Points**
- Rotavirus genotyping on the TAC card saves resources and has the goal of replacing genotyping at the RRLs.
- Sustainability of rotavirus surveillance needs to be considered since TAC is cost prohibitive for many countries.
- This is an urgent issue for regions to decide on to have the new TAC cards ready for 2019 testing.

**Norovirus genotyping by TAC and sequencing**  
*Presenter: Jan Vinje, U.S. Centers for Disease Control and Prevention*

**Presentation overview**  
There are several norovirus vaccine candidates in the pipeline. Understanding which strains are circulating globally and the variation of circulating strains by region is imperative in vaccine development and future vaccine effectiveness studies. CDC has developed an assay to sequence
norovirus samples and a standardized protocol for labs to use. Five kits were validated and compared, and the QIAGEN kit was found to be the best. Uploading of experiment data onto a web-portal, NoroSurv, automatically compares the sample sequence to reference sequences and determines the genotype. The portal includes features to view norovirus genotype distribution by country and time and is limited in access to those with a login code. Preliminary results for several countries were presented. Results will be compiled and distributed to WHO HQ and RRLs.

Discussion and Action Points
- Funding for norovirus sequencing is not guaranteed.
- Concerns about the data sharing of sequences of human samples; need to clarify issues such as who owns the data portal and sharing of sequences with gene banks.
- There has not been a multilateral agreement through the Nagoya protocol on whether sequencing data will be included for fair and equitable sharing of genetic resources. A survey will soon be distributed by HQ to all regional coordinators involved in WHO VPD laboratory networks. This will be an opportunity for everyone to provide feedback and opinions on what entails pathogen sharing as well as their access and benefit sharing arrangements.
- Countries waiting to receive individual reports of norovirus sequencing results.

Polio inactivation in context of containment: update
Presenter: Mike Bowen, U.S. Centers for Disease Control and Prevention

Presentation overview
The WHO Global Action Plan is a strategy to reduce the risk of poliovirus leakage after the eradication of wild poliovirus and the stoppage of oral poliovirus vaccine. The strategy includes destroying all potentially infectious materials (PIM) in all facilities (except poliovirus-essential facilities). Given that this would result in the loss of stool sample collections from rotavirus surveillance, a method is needed to inactivate poliovirus in the stool while maintaining ability for future testing of the stool. Through much experimentation, CDC has found that the use of GuSCN-based buffers with the addition of EtOH is a viable method for inactivating poliovirus while maintaining the integrity of nucleic acid in the stool for future testing. These buffers are already in commercially used kits, including the QIAGEN Viral RNA kit and UNEX buffer, which are in use at many laboratories in the WHO Global Rotavirus Surveillance Network, making them easily assessible. Further work by the CDC will determine the minimum concentrations of buffer needed and the minimum contact time. The lab will also work to evaluate methods for long-term preservation of stool specimens.

Discussion and Action Points
- CDC should record composition of buffers that work in case the company that produces them were to go out of business.
- The buffer is extremely useful to inactivate poliovirus in the stool and is much cheaper than the alternative of extraction.
- Some regions are pushing to destroy samples to avoid the issue of poliovirus in the stool, so there is an urgency in developing and disseminating a strategy for polio containment.

Day 2, Session II: Interpreting surveillance data: Controls and Mortality

Report from Enterics Burden Working Group: Systematic literature reviews of controls and mortality
Presenter: Mateusz Hasso-Agopsowicz, WHO HQ
Presentation overview
Product Development Vaccine Advisory Committee 2018 recommended the formation of Enterics Burden Working Group to investigate differences between enteric mortality estimates, primarily the discrepancy in global Shigella and ETEC mortality estimates. The working group has three workstreams: (1) systematic literature reviews of odds ratios and case fatality rates to identify areas where additional evidence is needed to improve future estimates, (2) a grading analysis and sensitivity analysis to understand the quality of studies included in the burden modeling, and (3) a comparison, meta-analysis, and sensitivity analysis to understand similarities and differences in IHME model input data and MCEE model input data. While the review of controls captures many geographically diverse studies, there are no EMRO, EURO, or Central America data, and very limited AFRO data. The three workstreams all have goals to be completed by March to June of 2020. While the working group is currently focused on mortality estimates, there is interest to expand the analysis to morbidity estimates as well.

Synthetic controls and potential control enrollment
Presenter: James Platts-Mills, University of Virginia

Presentation overview
The Global Enteric Multicenter Study (GEMS) and the Etiology, Risk Factors, and Interactions of Enteric Infections and Malnutrition and the Consequences for Child Health and Development Project (MAL-ED) are two landmark pediatric diarrhea etiology studies. Currently, controls from GEMS and MAL-ED are being used to assess the relationship between pathogen quantity and diarrheal disease in GPDS. While developing a cutoff for attribution of rotavirus is relatively straightforward, it is not as simple with other pathogens, notably norovirus, because of high rates of asymptomatic carriage and shedding. Additionally, the distribution of quantity of a pathogen appears to vary by region, so using GEMS and MAL-ED controls that were collected from Africa, Asia, and South America may not be applicable to other regions. One option is to continue to use the GEMS/MAL-ED models and understand that the estimates are likely conservative. Another option is to use propensity weighting or develop ‘synthetic’ controls to try to account for differences in controls from one region versus another; however, current attempts so far have not been successful. It is up for debate whether enrolling controls from some GPDS sites should be undertaken to help answer this question; however, consideration must be taken in how these controls would be used and if the benefit from including them is worth the time and effort it would take.

Discussion and Action Points
• Regions feel that is feasible to enroll controls if provided the funding and resources necessary to do so. However, we must consider the time and logistics involved in changing the protocol and getting approval from the Institutional Review Board that can be challenging.
• Before enrolling controls there needs to be thoughtful discussion of the use of the data and practicality of enrolling the controls. UVA will first simulate controls for proof-of-concept and they will share preliminary results to decide whether enrollment of controls is needed.

Mortality from rotavirus and pediatric diarrhea
Presenter: Rachel Hartman, WHO HQ and Johns Hopkins Bloomberg School of Public Health

Presentation overview
Using GPDS and GRSN data, an analysis was performed to look at the association between pediatric diarrhea and mortality. The overall case fatality rate was found to be 0.5%. A multivariate regression was fit to evaluate odds ratios of death. Younger cases have a higher odds of death than older cases, and female cases have a higher odds of death than male cases. Cases in the AFRO region have the highest odds of death, and cases in the EURO region have the lowest odds of death. Persistent cases have a higher odds of death than acute cases. Cases without vomiting have a higher odds of death than cases with vomiting. Cases with severe dehydration have higher odds of death than cases with no or some dehydration. Rotavirus negative cases have higher odds of death than rotavirus positive cases. Further analysis will assess if there are regional differences in risk factors and investigate attributable pathogens in TAC-tested samples of cases who died.

Discussion and Action Points
- Assess time until death to see if most of the deaths are occurring soon after a child is admitted to the hospital or after admittance.
- When looking at hospital deaths, it may not be surprising that rotavirus positive cases have lower odds of death than rotavirus negative cases, since rotavirus deaths are most commonly from dehydration which can be managed if a child presents to a hospital.
- Sex pattern observed could be in part due to female children being brought to care later than male children, therefore leading to female cases having higher odds of deaths.

Updated global rotavirus mortality burden estimates
Presenter: Jackie Tate, U.S. Centers for Disease Control and Prevention

Presentation overview
Previous rotavirus mortality estimates were published in 2016 using data from 2000-2013. Major findings were that the proportion of deaths due to rotavirus declined slightly from 43% in 2000 to 37% in 2013. Four countries (India, Nigeria, Pakistan, and DRC) accounted for approximately half of all deaths. The estimates were developed using a literature review to identify data and constructing a multiple linear regression model, considering rotavirus vaccine introduction status. CDC is in the process of updating these mortality estimates to include data through 2018; results are expected to be available for review in Q2/Q3 of 2020.

Day 2, Session III: Future directions for Rotavirus and Pediatric Diarrhea Surveillance

Discussion and Action Points
- Important for countries to receive data in a useful and timely way and need to consider if there are additional analyses of data that countries are interested in receiving. As part of capacity building, countries should also be given the opportunity to learn how to conduct these epidemiological analyses so they can present and disseminate their own findings.
- Network can be used as an example for comprehensive VPD surveillance to help advocate for funding.
- Representatives from PAHO countries expressed high commitment to rotavirus surveillance, the need for funding and regional support to continue this surveillance, and the importance of the data being shared with the countries. These data are critical for presenting to their Ministries of Health to provide evidence that maintaining surveillance is a key activity in public health.
• There is a big concern that if countries lose national and/or external funding for rotavirus surveillance, other priorities will result in countries ending rotavirus surveillance even before vaccine introduction.

Next Steps
• WHO HQ will circulate the revised site assessment tool for use and feedback.
• Since the pilot laboratory data EQA exercise was successful, the exercise will be continued next year and expanded to include all RRLs. Sites with poor performance will be prioritized for trainings and site visits.
• WHO Regional Offices and RRLs will work to standardize IDs used in surveillance and TAC data to assist in the process of linking the clinical and laboratory data.
• New proposed TAC card layout will be shared with justification for inclusion and removal of targets. Regions and countries will discuss and return feedback to WHO HQ and University of Virginia.
• WHO Regions will discuss further with RRLs on the timing and frequency of sample shipments as well as timing of TAC testing. They will return a proposed plan to WHO HQ in Q1 2020.
• Before deciding whether to enroll controls for GPDS, the University of Virginia team will use simulate whether adding controls will affect estimates to provide a proof-of-concept and WHO HQ will investigate if there are contemporary studies with collected stool samples that could just be tested by the network to save time and resources.
• Norovirus genotyping results will be distributed to countries.
• A protocol for poliovirus inactivation will be developed by CDC GRL and circulated to labs.

Meeting agenda and list of participants follow.
Global Rotavirus and Pediatric Diarrhea Surveillance Meeting  
19-21 November 2019  
JW Marriott Hotel, Rio de Janeiro, Brazil

Agenda

Objectives:
- Review data from Global Rotavirus (10 years) and Pediatric Diarrhea (2 years) Surveillance
- Discuss priorities and future activities for rotavirus and pediatric diarrhea surveillance

**Tuesday, 19 November 2019**  
*Participants: All*

**Chair:** Umesh Parashar  
**Rapporteurs:** Rachel Hartman and Heidi Soeters

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<td>• Importance of data quality management (15 min)</td>
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<td>• Quality assurance systems (EQA, EQC) (15 min)</td>
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<td>14h15-15h15</td>
<td>• Do we need a GPDS laboratory site and RRL assessment tool?</td>
<td></td>
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<tr>
<td>15h15-15h45</td>
<td>Coffee break/Tea Break</td>
<td></td>
</tr>
<tr>
<td>15h45-16h30</td>
<td>Performance and support: Regional and global experience</td>
<td>Lúcia de Oliveira Emmanuel Tondo</td>
</tr>
<tr>
<td>15h45-16h30</td>
<td>• Surveillance experience from PAHO (15 min)</td>
<td>Ibrahim Khalil</td>
</tr>
<tr>
<td>15h45-16h30</td>
<td>• SEAR perspective on two new rotavirus vaccines in India (15 min)</td>
<td></td>
</tr>
<tr>
<td>15h45-16h30</td>
<td>• Advancing enteric vaccines and Full Value of Vaccines Assessment (15 min)</td>
<td></td>
</tr>
<tr>
<td>16h30-17h00</td>
<td>Discussion and Day 1 wrap-up</td>
<td></td>
</tr>
<tr>
<td>17h30-19h00</td>
<td>Reception</td>
<td></td>
</tr>
</tbody>
</table>
### Wednesday, 20 November 2019

**Participants:** All

**Chair:** Carl Kirkwood  
**Rapporteurs:** Rachel Hartman and Miren Iturriza-Gomara

#### 9h00-9h45  
**Laboratory technical considerations**  
- Composition of new GPDS TAC card layout (10 min)  
- Rotavirus TAC genotyping validation (10 min)  
- Inactivation of Poliovirus in Potentially Infectious Material Project Update (10 min)  
- Norovirus genotyping by TAC and sequencing (15 min)  
  
<table>
<thead>
<tr>
<th>Darwin Operario</th>
<th>Mathew Esona</th>
<th>Mike Bowen</th>
<th>Jan Vinje</th>
</tr>
</thead>
</table>

#### 9h45-10h45  
**Discussion questions**  
- Do we have consensus of new TAC layout and assays?  
- What is way forward for rotavirus genotyping?  
- What is way forward for norovirus genotyping?  
  
| Group discussion |

#### 10h45-11h15  
**Coffee/tea break**

#### 11h15-11h55  
**Interpreting surveillance data: Controls and Mortality**  
- Report from Enterics Burden Working Group: Systematic literature reviews of controls and mortality (10 min)  
- Synthetic controls and potential control enrollment (10 min)  
- Mortality from rotavirus and pediatric diarrhea (10 min)  
- Updated global rotavirus mortality burden estimates (10 min)  
  
<table>
<thead>
<tr>
<th>Mateusz Hasso-Agopsowicz</th>
<th>James Platts-Mills</th>
<th>Rachel Hartman</th>
<th>Jackie Tate</th>
</tr>
</thead>
</table>

#### 11h55-12h30  
**Discussion questions**  
- Are synthetic controls sufficient?  
- Should we identify sites to enroll controls?  
- What are the needs for updating mortality estimates?  
  
#### 12h30-13h30  
**Lunch break**

#### 13h30-14h30  
**Future directions for Rotavirus and Pediatric Diarrhea Surveillance**  
- Are we getting useful data from the surveillance?  
- What other data or analyses are needed?  
- What are future directions for ongoing surveillance?  
  
| Small group discussion |

#### 14h30-15h00  
**Report back and wrap-up**

#### 15h00-15h30  
**Coffee/tea break**

#### 15h30-17h30  
**WHO Closed Session**

### Thursday, 21 November 2019

**WHO Closed Session (morning): Participants:** WHO  
**Regional Reference Laboratory tour (afternoon): Participants:** Open to all

**Chair:** TBD  
**Rapporteurs:** TBD

#### 9h00-10h30  
- WHO Closed Session

#### 10h30-11h00  
**Coffee/tea break**

#### 11h00-12h30  
- WHO Closed Session

#### 12h30-13h30  
**Lunch break**

#### 13h30-17h00  
- Regional Reference Laboratory tour
Global Rotavirus and Pediatric Diarrhea Surveillance Meeting  
18-21 November 2019  
Rio de Janeiro, Brazil  
Marriott Rio Hotel

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