The 20th Informal Consultation of the Global Polio Laboratory Network.

26-27 June 2014, WHO Headquarters, Geneva, Switzerland

FINAL REPORT

The 20th Informal Consultation of the WHO Global Polio Laboratory Network (GPLN) was held in Geneva, Switzerland, on 26-27 June 2014. The meeting included participants from laboratories of the six WHO geographical regions including WHO Laboratory Coordinators and representatives of the 146 member laboratories of the GPLN. The main discussions focused on laboratory issues of relevance to the Global Polio Eradication Initiative (GPEI) with an aim to establish technical priorities and policies to ensure that all laboratories of the GPLN operate with accuracy and efficiency in their critical role of confirming the presence/absence of poliovirus (PV) in samples from all surveillance activities. The molecular characterisation of PV isolates by laboratories of the GPLN provides essential information for the epidemiological analysis required to understand the PV natural history to help establishing the temporal and geographical PV transmission pathways.

A. GLOBAL AND REGIONAL UPDATES ON WPV AND VDPV TRANSMISSIONS

Dr Bruce Aylward, WHO Assistant Director General, opened the meeting by thanking the GPLN for their excellent performance, essential for guiding the progress of the GPEI. Dr Hamid Jafari, WHO Director a.i of Polio Operations and Research, reviewed the current state of the GPEI giving an overview of the performance, activities and challenges faced by the Programme and describing planned Endgame strategies and current priorities for the programme. The WHO Global and Regional Polio Laboratory Coordinators presented detailed information on the performance of polio laboratories from the different regions, providing data on the detection and molecular epidemiology of

wild polioviruses (WPVs) and vaccine-derived polioviruses (VDPVs) isolated from the different surveillance activities.

Although important progress has been made in recent years in terms of reducing the extent of endemic areas and limiting the number of genetic clusters of circulating WPVs, there are still important challenges and concerns that remain to achieve global polio eradication. Transmission of WPV1 is still endemic in three countries: Nigeria, Afghanistan and Pakistan with the number of cases decreasing in Nigeria and Afghanistan but increasing in Pakistan. The large outbreak occurring since April 2013 in Kenya, Ethiopia and Somalia due to WPV1 of Nigerian origin, seems to be at its last stages although recent isolations of related WPV1s in Ethiopia and Somalia indicate that there is still active transmission of the virus in some areas. Importation of WPV1 originally from Pakistan has been detected in various countries during 2013-14 with related WPV1 isolates found in environmental samples in Egypt and Israel and polio cases reported in Syria and later in Iraq. A separate importation event has been described in Cameroon and Equatorial Guinea also in 2013-14, with several paralytic cases linked to WPV1 strains. The closest sequence matches to these viruses correspond to WPV1s found in Chad in 2011 signaling important gaps in surveillance and undetected transmission in those areas. It is not clear where and when WPV1 closer ancestors of WPV1s found in Cameroon and Equatorial Guinea circulated during this long “silent” period of more than two years. A WPV1 strain, closely related to isolates from Equatorial Guinea, was found in sewage samples in Brazil in March 2014, which clearly shows that there is still a global risk of WPV importation. Furthermore, small outbreaks due to circulating VDPV2 continue to occur in different parts of Central Africa and Pakistan. Evaluation of surveillance performance indicators showed that the main reason for WPV circulation and paralytic cases still occurring in some areas continues to be failure to immunize large numbers of children due to the deterioration of public health services, armed conflict or civil unrest. Active efforts to close these gaps and interrupt PV circulation in all these areas are on course with immunization campaigns and enhanced surveillance activities being implemented.

Current status of projects aiming to provide information and knowledge to update relevant GPLN guidelines and documents such as the Polio Laboratory Manual, Accreditation Checklists and the Global Expansion Plan for Environmental Surveillance, were presented. Important progress has been made in these tasks which will hopefully be completed soon. In particular, environmental surveillance (ES) will be of major importance in the next few years as it is seen as a powerful and sensitive tool to detect PV circulation even in the absence of paralytic cases. VDPV isolates containing highly drifted VP1

sequences from Sabin and presumably excreted by unidentified immunodeficient individuals have also been often detected in ES samples from various countries. WHO Coordinator for Polio Surveillance, Monitoring and Information, described the main content of the Global Expansion Plan for ES for 2013-2018, which promotes the use of ES to help identifying residual transmission in endemic areas and providing an early indication of new importations into recurrently re-infected locations. The plan is to maintain current ES activities and to expand them to new sites in high-risk areas along routes of WPV importation and selected areas where populations at a particular risk of VDPV emergence. ES will also be very useful in assisting, monitoring and documenting the elimination of Sabin viruses following the tOPV to bOPV switch and, eventually, the total cessation of OPV use. Consequently, environmental sampling sites in at least 15-20 additional cities and locations will be added globally, prior to the planned tOPV-bOPV switch expected to occur around mid-2016. Data from ES will be used as supportive documentation for the certification of polio eradication.

Presentations and discussions were also held on the progress of the development and evaluation of new diagnostic reagents and approaches such as the use of new testing algorithms for rRT-PCR ITD or ES, the direct detection of PV in stool and sewage samples using PV-particles concentration techniques and the finding of WPV in sewage samples during an outbreak context in Israel. An important step was consensus on a new algorithm for ES (from concentration using double-phase method to virus isolation and characterization using the new rRT-PCR ITD algorithm). As usually done during the annual global meeting, thorough reviews of the GPLN's quality assurance program were presented by scientists from GSLs with information and conclusions on the results from annual proficiency testing activities used to assess the performance in the different laboratory techniques. Quality assurance is one of the strengths of the GPLN and, as in previous years, performance during last year has been excellent. Most laboratories of the GPLN, with only few exceptions, are fully accredited to perform the required functions. However, an important set-back occurred in 2013 as South Sudan was erroneously declared infected with WPV1 related to isolates found in the outbreak in Kenya, Somalia and Ethiopia. This explosive outbreak resulted in a significant increase in workload that stretched resources at the Kenya NPL laboratory to their limit. There was a major increase in AFP samples for testing and the laboratory infrastructure was not able to cope with the testing demand. As a consequence, a backlog of samples for testing accumulated and the laboratory quality indicators dropped, particularly those related to timelines for PV isolation and characterization. This difficult situation was likely one of the main reasons that led to the cross-contamination of stool samples from

South Sudan which were initially identified as positive for WPV1 genetically linked to outbreak strains. However, a thorough investigation including nucleotide sequence comparison between WPV1 isolates obtained in the same laboratory and scrutiny of laboratory records clearly identified the virus isolates from South Sudan as cross-contamination from samples from Somalia that had been handled in the same laboratory area at the same time. This prompted a major review of procedures at Kenya NPL that identified deficiencies in many aspects of the whole process of virus isolation which included those affecting shipment and receipt of stool specimens, labeling and assigning EPID codes to samples, laboratory infrastructure such as space in incubators for cell cultures and overall human resources and supervision management of the situation. Corrective actions were proposed and immediately implemented. This experience by the Kenya NPL laboratory highlighted the need for contingency plans at regional level and in all laboratories to anticipate increase in workloads and propose alternative plans e.g shifting some samples to other polio laboratories. This incident however shows that despite this deficient performance at a particular time the GPLN has adequate mechanisms to promptly review and correct the situation. Indeed the NPL Kenya has been able afterwards (samples from South Sudan shifted to Uganda NPL) to satisfactorily handle this extensive outbreak.

Since last meeting the security situation has deteriorated in several endemic/outbreak countries (Nigeria, Pakistan, Afghanistan, Syria, Irak and Somalia). It has been stressed out that despite serious challenges the GPLN laboratories located in these countries were able to maintain high commitment and high quality standards resulting in production of accurate and timely results that helped the programme to implement appropriate actions to control WEPV transmission in these areas.

B. REVIEW OF 25 YEARS OF THE GPLN AND PROSPECTS:

This year marks the 25th anniversary of the GPLN. Dr Mark Pallansch and Dr Olen Kew from US CDC, gave tribute to this landmark during the meeting and described the content of the original Plan of action for the laboratory activities to support the GPEI that they discussed with WHO and wrote during a visit to Geneva in 1989. All essential elements currently used in the GPLN were in the original plan. The initial vision was for a dynamic network, including the flexibility to develop and adopt improved methods and innovation. A three-tier structure with different levels of responsibilities and specific lines of communication and reporting, very similar to that used today, was proposed. The aim was to achieve high levels of performance which would be accomplished by developing standardized methods in collaborative studies, by organizing workshops for training activities and by holding regular meetings

to discuss progress, constraints and needs as well as to exchange experiences and solutions. The close integration between surveillance and laboratory activities, which has proven essential to ensure the effectiveness of the GPEI, was also viewed as one of the essential goals of the plan as it would ensure that the data generated from virological and epidemiological work were available as the basis for action by managers of immunization programmes. The GPLN today includes a consistent number of laboratories (146) with diverse but well-defined roles and functions. Tribute was paid to former global coordinators (three of them were invited for this meeting) who largely and efficiently contributed to build the network.

As ever, laboratories of the GPLN have proven their capacity to adapt to changing situations to ensure their continuous and effective support to the GPEI. An example being the recent introduction of new molecular techniques and an increased complexity in laboratory testing, such as the use of different procedures required to reach comprehensive characterization of a PV isolate or the testing of samples other than those from AFP surveillance such as those from environmental samples, stool surveys, clinical studies, etc.

In light of the recent adoption of the Polio Eradication Endgame and Strategic Plan (PEESP) for 2013-2018, one of the main tasks for the GPLN will be to ensure that laboratory procedures and work practices are in line with the PEESP's objectives to better inform and orient the GPEI in its mission to detect and interrupt PV circulation, to strengthen immunization systems and support the withdrawal of OPV for immunization, to certify PV eradication and achieve PV containment and to plan the use of the vast experience developed by the GPEI as a legacy for other public health programs to control and eliminate infectious diseases. In addition, on 26th April 2014, following the international spread of polio during 2014, the WHO International Health Regulations Emergency Committee declared the situation with polio as a Public Health Emergency of International Concern (PHEIC) as "it constitutes an 'extraordinary event' and a public health risk to non-infected States for which a coordinated international response is essential". The declaration of a PHEIC for polio added yet more pressure to the GPLN in its efforts to continue to support the GPEI in a very challenging situation.

It is noteworthy that numbers of scientific projects conducted by laboratories inside (mainly) and outside the GPLN are also contributing to different aspects of the Endgame. These include studies on population seroprevalence, clinical studies to assess different vaccination strategies and development of new products to improve polio immunization and prophylaxis such as antivirals, vaccine adjuvants or safer vaccines for the post-eradication era.

SWOT ANALYSIS

During the meeting, a SWOT (Strengths, Weaknesses, Opportunities and Threats)" analysis based on the 25 years of GPLN's experience was conducted. Participants were divided in groups to discuss the main achievements and constraints of the GPLN during this period and to identify opportunities for development and threats for its sustainability with an aim to determine concrete actions to improve performance in the context of the PEESP.

Participants were distributed in four groups and asked to identify and get consensus on the main Strengths, Weaknesses Opportunities and Threats for the GPLN in the context of the Endgame for the GPEI. All participants shared the findings from each group, discussed ranking of opportunities and threats and agreed on key action-points/activities to be conducted in the short-term to close gaps and/or better meet programmatic needs. The summary of findings and recommended actions identified during this exercise is shown below. A Word Cloud analysis representing the most frequent words mentioned by all groups during the analysis is shown in the Figure below. As shown, same words were often mentioned in different sections. This is not unexpected as, for example, communication within the GPLN was seen as strength but poor communication between the GPLN and some areas of the GPEI was perceived as a weakness. There was also some overlapping between sections as, for example, lack of human and financial resources was identified both as a weakness and a threat for the GPLN.

1. Strengths

- Strong network structure – built over the years (Served as model for other networks and will be a key component of GPEI legacy after certification of eradication)
- Efficient collaboration/co-ordination at different levels within the network
    - Strong foundation
    - Excellent support
- Integration with EPI programme
- High competency and reliability
    - Methods, procedures and Technologies
    - Quality assurance at all steps to ensure accuracy
    - Strong data management

2. Weaknesses

- Resources:
    - Budget constraints
    - Human resources: staff turnover
    - Lack of national/political support
- Lack of managerial skills at laboratory level
- Insular:

    - Poor communication with non-GPLN laboratories
    - Poor communication between regions at laboratory level
    - Poor communication with general public
    - Poor communication with EPI in some instances
- Incomplete documentation of some unexpected events to be used to improve performance (lessons learnt not widely disseminated)

3. Threats

- Sustainability:
    - Human resources - Staff attrition
    - Maintaining/acquiring competency (rapid development of new technologies)
    - Lack of resources - budget
    - Competing priorities
    - Post-eradication
- Security
    - Political situation
- Logistics:
    - Transport of samples between laboratories
    - Stringency of national/international regulations

4. Opportunities

- Integrated disease surveillance:
    - Global integration with EPI and other programs
- Adaptation and continuous evolution:
    - Adoption of new technologies
    - Re-structuring of the network
- Diversification of activities:
    - Contribution to PV containment
    - Environmental surveillance
- Legacy planning:
    - Leadership
    - Contribution to International Health Regulations (IHR)

5. Priority actions identified

1. Facilitate diversification and staff development:
    a. Training of staff
    b. Management courses for laboratory managers
    c. Promote individual recognition to prevent staff attrition
2. Establish clear budget plan to support expansion of capacity
3. Showcase GPLN contribution to the success of the GPEI:
    a. Promote success visibility: recognition and visibility by all stakeholders, within and outside WHO
    b. Increase national ownership of achievements
    c. Educate the next generation of virologists and epidemiologists on polio as the best example for global step for VPD control
    d. Communicate with national authorities
4. Design a clear legacy plan:
    a. Develop an Integrated disease surveillance approach as part of the IHR

    b. Maintain polio laboratories' infrastructure, methodologies and QA processes as core facilities for public health programs after eradication
5. Make efforts to integrate all GPEI bodies such as national and regional certification committees, polio monitoring board, GPLN, etc. which should all be able to contribute to relevant decisions of the GPEI
6. Increase security measures:
    a. Contingency plan to relocate personnel and resources

C. <u>GROUP DISCUSSIONS</u>

Group discussions were also conducted on the impact and changing needs that the GPLN will need to deal with during the progressive phases of the GPEI Endgame. Three key priority areas where considered in which the support of the GPLN will be essential to guide policy decisions: the detection and characterization of PVs from different surveillance activities and sources; the laboratory containment of PVs; and the quality assured expansion of ES for PV detection. As the annual Informal Consultation of the GPLN gathers scientists from GSLs, RRLs and NLs, global and regional coordinators, as well as scientists and epidemiologists from WHO HQ, it is a very good opportunity to discuss these issues from different perspectives and to come up with common conclusions and action plans for the coming future.

Group 1: Poliovirus detection

The first group discussed the changes that will be required in diagnostic techniques for the effective detection, characterization and molecular epidemiological analysis of WPV, VDPV and Sabin strains at different stages of the Endgame.

The terms of reference were:

- to discuss improvements needed to align PV detection and reporting with the different phases of the Endgame strategic plan,
- VDPV characterization and reporting: discuss key principles and information exchange

The group agreed that improved and/or new technology will be needed to respond to the increasing demands that the GPEI will require as the Endgame advances. Laboratories of the GPLN led by CDC are actively working on the improvement and development of standards and protocols to satisfy these demands. The development of methods for the direct detection of PV from stool and environmental samples, equivalent or more sensitive to current methods based on cell culture, would be very useful. However, issues such as (i) the need to establish the quality assurance to support such methods, (ii) the logistics required for implementation of the techniques in all (146) laboratories of the GPLN and, (iii)

technical concerns such as the stability of nucleic acid in clinical samples, would need to be resolved before such methods are fully implemented. The programmatic significance of finding PV nucleic acid sequences in the absence of infectious PV was also discussed. It is expected that additional financial and human resources for increasing testing demands will be required particularly for selected laboratories that will be testing samples in the latest phases of the Endgame.

A key step in the Endgame strategic plan will be the cessation of OPV2 use for immunisation. For this to happen, the GPEI needs reassurance that no cVDPV2 strain is circulating anywhere in the world. The GPLN needs to evaluate current methods for such purpose by reviewing known examples where transmission might have been missed and identifying ways to correct deficiencies. It will be important to establish measurable indicators to confirm that circulation of PV2 have been actually interrupted. ES could be a very valuable tool to help monitoring the disappearance of PV2 circulation but it needs to be implemented following recommended guidelines so that the provided information is meaningful to the GPEI.

In this context, the final classification of any PV strain as a cVDPV becomes a very high profile decision; so effective communication between the GPEI and the GPLN is essential. For this reason, detailed guidelines for the reporting and classification of VDPVs are being drafted by WHO HQ. The group made suggestions for some changes in the document as well as for changes in the associated VDPV reporting template. The main recommendation from the group was that the GPEI Surveillance group, with advice from the GPLN, should arrange and supervise all field activities and necessary actions required for establishing the final classification of any VDPV isolate as circulating (cVDPV), from an immunodeficient patient (iVDPV) or ambiguous (aVDPV).

Following cessation of OPV2 use, it will be important to monitor closely the disappearance of PV2 analysing the possible evolution of genetic clusters. There is also a need to develop a programmatic response to any VDPV2 isolation both at the GPEI and GPLN level: what testing will be required, which samples need to be tested, when and what immunisation response should be implemented, etc. The group agreed that the time to start a more in-depth analysis and real-time reporting of PV2 isolations is 6 months after interruption of OPV2 use. After this time, any PV2 isolation should be considered an emergency and full characterisation and accurate reporting will be considered a very urgent matter. At present, polio certification is planned as a two-stage program with PV type 2 to be certified first followed by type 1 and type 3 together. However, given the fact that no WPV3 has been isolated for more than two years and WPV1 is still circulating in various areas of the

world, a contingency plan is needed in case a three-stage plan is required. In this case, OPV2 will be withdrawn from the vaccine first followed by OPV3 and finally OPV1. At present, methods to detect Sabin 3 PVs are adequate but methods to specifically identify VDPV3 strains (sequencing excepted) are still not fully optimised.

The group proposed following action points:

- Resources needed for capacity building in the GPLN in preparation to meet the needs of polio eradication phases should be identified
- Studies using available collections of stool/environmental samples should be conducted to compare the sensitivity of molecular assays versus virus isolation in cell culture
- Data from historical and recent vaccine trials could be used to further establish the duration of OPV2 excretion following immunisation
- The guidelines for the reporting and classification of VDPVs should be finalised
- There should be close communication between the GPEI Surveillance group and the GPLN to establish the final classification of VDPVs, to monitor the disappearance of PV2 circulation after OPV2 cessation and to plan any necessary programmatic actions following PV2 isolations
- ES in key geographical areas can address broader populations and should be intensified in areas with recent VDPV isolations
- Screening of individuals with primary immunodeficiencies for PV excretion should be intensified with the GPLN offering assistance for laboratory testing
- After 6 months of OPV2 cessation, laboratories should send an intermediate report to the GPEI with details on PV2 isolations including molecular information
- Establishing a mechanism for sharing nucleotide sequence information of representative circulating PVs within the GPLN would be very useful to quickly determine molecular epidemiology links between PV isolations.

Group 2: PV Containment

The second group discussed the roles and requirements for the GPLN to facilitate and support laboratory containment of PV at different stages of the GPEI Endgame

The terms of reference were:

- To identify critical steps and activities for the containment of PV in GPLN laboratories.
- To align the activities of GPLN laboratories on PV containment with the GAP-III document.

Laboratory containment for PV is planned as a multi-stage process with different categories of PV aimed for containment at different stages. It needs to be in line with the different phases of the Endgame determined by the step-wise completion of polio certification and subsequent changes in immunisation policies. Containment of WPV2 should be immediate but it is not likely to be a major challenge as no WPV2 has been isolated since 1999 and very few laboratories hold or work with WPV2 strains today. However, VDPV2 isolates can be considered as WPV2 in terms of containment and their containment within the required timelines will be more problematic as there are still some on-going outbreaks due to VDPV2 strains. VDPV2 strains can also be present in recent clinical and environmental samples alone or in mixtures with other WPVs or even in contemporary samples from non-polio patients. Type 2 strains are also the most common VDPV strains shed by long-term excreters' immunodeficient patients which represent another major challenge for containment. Similarly, containment of WPV1 and WPV3 will also be complex as they are required to be contained within one year of eradication. WPV3 was last seen in November 2012 and WPV1 is still circulating in parts of Central Africa, Horn of Africa and Pakistan/Afghanistan.

When considering historical collections for possible containment, including samples collected for other purposes than PV isolation, there should be a balance between risk and feasibility. Laboratories should focus on samples with the highest risk such as stool samples contemporary with and geographically linked to areas of known circulation of WPV. Points for consideration when deciding what polio samples to destroy and what samples to retain are the availability of nucleotide sequences and the programmatic importance of the stored isolates.

The need for serotype-specific containment at different stages of the Endgame will represent a major challenge as, for example, samples containing Sabin mixtures might contain Sabin 2 strains below the detection threshold as can be found when using more sensitive molecular techniques.

In essence, the group perceived that there should be a right balance between the complexity of the process set up by GAP-III and the need to maintain high levels of safety as there will be a need for changes in behaviours to meet the new requirements.

A small number of essential facilities will be selected to handle PV during the latest phases of the Endgame. These facilities will need the support and approval of National Authorities that are willing to support the process of containment and accreditation. Laboratories dealing with the isolation and characterization of PV from clinical and environmental samples should probably be selected from the current GPLN as it will be highly impractical to set up new laboratories for this purpose. A number

of aspects will also need to be considered when selecting these laboratories such as the need for national and international accreditation processes, the levels of staff immunity required to prevent transmission, the mechanisms to follow if contamination occurs and the training requirements on biosafety and biorisk management for laboratory workers and managers. Provision for the safe handling of samples in non-essential facilities should also be made since samples containing PV might be first handled in such facilities before being shipped to an essential laboratory. The challenges derived from synthetic biology were also mentioned as some research groups might still be handling nucleic acid materials containing PV sequences which can be easily used to generate infectious PV.

Most regions have completed the first phase of containment which involved preparing a survey and inventory of all facilities holding infectious or potentially infectious WPV materials. All countries in EUR, AMR, SEAR and WPR have completed the survey. All countries except Pakistan, Afghanistan and Somalia in EMRO and 8 countries in AFR have also accomplished the first phase.

A number of action points were proposed with the aim to simplify the process and highlight the role of the GPLN in PV containment:

- The completion of regional inventories should be accelerated ensuring that all regions conduct regular revisions and updates of their inventories
- Provision of a digitalized inventory of global facilities working with PV should be considered. Member States should have access to this global database and updates should be submitted annually to the Regional Certification Committees
- Communication between all partners directly involved in containment including the National Polio Containment Coordinators, the GPLN, WHO RO and HQ, etc. are essential for the effective completion of PV containment
- Any changes in containment guidelines should be reflected in National Regulations. Member States need to provide comments and points for consideration before endorsement by the WHA
- There is a need for clear and concise instructions to Member States and facilities holding PVs, including vaccine production sites, on what samples to destroy and when
- As important stakeholders of the GPEI, the GPLN should lead by example the process of polio virus containment.
- Guidelines on how to implement and document PV containment should be made available to all facilities holding PVs or potentially infectious materials

- Instructions for the destruction of PVs and potentially infectious materials and for the certification of this process should be given to facilities holding PVs or potentially infectious materials and the corresponding authorities
- Mechanisms for the accreditation of facilities selected to work with PV at different stages of the Endgame should be developed
- The tier of responsibilities to oversee the containment process are still to be determined at the higher National and International levels following the revision of GAP-III
- Biosafety and Biosecurity safeguards required to work with PV at different stages of the Endgame should be identified
- Combining the containment of WPV2 and WPV3, and even of WPV1, at the same time should be considered as it will simplify the process and reduce safety risks
- The research community should be made aware of the implications of containment requirements for their work including the use of synthetic nucleic acid materials in the laboratory. Safeguards necessary to minimise risks from this area should be defined
- Laboratories of the GPLN should give feedback on the GAP-III draft document including the proposed definitions, step processes and timelines and recommendations on biorisk management in the context of the PEESP
- The Global GPLN coordinator should consider including some of these points as part of recommendations from the Informal Consultation meeting

Group 3: Environmental Surveillance

The third group discussed on GPLN plans to improve ES for PV and support the global expansion plan. The terms of reference were:

- To discuss global needs in terms of planning and implementing ES for PV.
- To define rationale for incorporating new sites/countries.
- To define timeline and approach for laboratory capacity building (diagnosis) and Quality Assurance (QA) in relation to the PEESP and GAP-III.

The group recognizes the importance of ES at this stage of the GPEI and the urgent need for actions to help expansion, standardisation and quality assurance of ES procedures.

A limited number of laboratories will be selected from each WHO Region to perform ES. The selection of new sites will be based on programmatic priorities. Sites will include those in current endemic

countries, recently re-infected countries, high risk countries and IPV using countries with high levels of immunity. One of the major limitations will be transportation of sewage raw materials to some laboratories (within the same country and between countries) For this reason, provision will be made for some laboratories to perform only the sewage concentration step, particularly in regions or countries where there is no accredited polio laboratory and known problems with transportation exist. The concentrated sewage can then be shipped to a polio laboratory in the same or other country for viral isolation and characterization.

Selected laboratories will be pre-assessed for their ability to perform the required functions. Evaluation of both the field and the laboratory components of the processes required for ES will be part of this assessment. This includes the evaluation of logistics such as site selection, sample collection and transportation and the suitability of laboratory facilities including the availability of dedicated space separated from AFP work in case of polio laboratories, the possibility of correct management of workflow and the provision of biosafety and biosecurity measures to control work practices. It is expected that the site selection, evaluation and monitoring will be done independently by a national surveillance group.

The next phase will be to build/enhance laboratory capacity and to implement ES laboratory procedures and work practices. The process will be ended by conducting on-site validation of the laboratory before it is established as a WHO ES laboratory. Ensuring both the human and financial resources required to support this work will be an important part of this process.

The plan is to evaluate the laboratory processes including those required for concentration, virus isolation and identification in order to develop standardised methods, quality assurance procedures and accreditation checklists specific for each category laboratory: concentration laboratory and polio (isolation and characterization) laboratory. This will include full assessment of work practices including storage of specimens and isolates, procedures for decontamination, interpretation of results, mechanisms for reporting, data management and preparation of an inventory of all equipment, consumables, reagents, diagnostic kits, etc. required for laboratory testing. This evaluation will also include requirements for biosafety and biosecurity associated with this work as well as training processes necessary to acquire and maintain competency in the different techniques. The results of this comprehensive evaluation will be used to prepare SOPs, identify performance indicators reflected in accreditation checklists and prepare proficiency testing strategies to assess laboratory performance

There is a need to develop a review process which might include not only the preparation of annual

quarterly report but also the independent assessment and regular review of sites, laboratories and sample transportation records. The accreditation plan will be pilot tested in a few laboratories before global implementation.

The group proposed following action points:

- A checklist with laboratory functions required for a facility to be designated as a WHO ES laboratory should be prepared before end of Q3 2014.
- Laboratories selected to perform ES of PV in the framework of PEESP phase 1, should be assessed for their ability to perform functions before Q4 2014.
- Quality assurance procedures for ES and a detailed accreditation process should be defined before Q1 2015.
- Plans for capacity building, implementation and on-site validation of ES in selected laboratories should be finalised before Q2 2015.

D. CONCLUSIONS

This 20th Informal Consultation of the GPLN has focused on identifying and discussing technical priorities and policies relevant to and necessary for an optimal functioning of the GPLN and its capacity to fulfill roles and responsibilities attributed by the GPEI. The performance of GPLN laboratories and implementation of quality assurance were reviewed and several areas of work were visited, with special emphasis on poliovirus (i) detection and reporting, (ii) containment and (iii) environmental surveillance.

As the GPLN is celebrating 25 years of existence this year, two innovations related to the format of the meeting were introduced :

(i) a SWOT analysis session which has permitted to take the opportunity to broadly identify key actions needed to maintain and develop, where need be, the capacities and efficiency of the GPLN to fulfill its mission, and

(ii) three group-work sessions devoted to the three areas of work listed above were held to foster discussions and key priority actions were identified and will be included in the GPLN agenda to support the 2013-2018 Polio Eradication and Endgame Strategic Plan.

E. RECOMMENDATIONS

1. PEESP in PHEIC context

Recognizing that recommendations and targets set up by the PEESP and PHEIC implications are likely to result in increased pressure on the GPLN, there will be a need for improved communication, coordination and cross-regional collaboration.

- Laboratory Directors should be guided to prepare, in coordination with the Regional Coordinator and National Authorities, a contingency plan to respond to unforeseen increases in workloads due to a polio outbreak, equipment failure and/or an increase in surveillance activities. The contingency plan should include all aspects that contribute to successful laboratory performance and might have an impact during emergencies such as human resources, facility, supplies, testing strategy, data management, communication, coordination, funding and biorisk measures.
- Laboratories (mainly those serving endemic and outbreak countries) should pay attention for timely sharing information and materials. The interpretation of molecular epidemiological data generated by laboratories should be coordinated by Regional/Global Laboratory Coordinators and scientists from the GSLs to ensure that accurate chronological and geographical links are

established between PV isolates from different areas, countries or regions as this provides essential information to guide GPEI activities.

- There is a need for a comprehensive inventory of diagnostic laboratories outside the GPLN that might isolate PVs. Efforts should be made to increase collaboration with non-GPLN laboratories prioritizing the need for fast and accurate PV isolation and characterization

2. Revision of Polio Laboratory Manual (PLM)

- The SWG should submit updates by July 8, 2014 so that a consolidated draft can be circulated by 31 July 2014 and reviewed by 30 September.

3. Revision of accreditation checklists for Virus Isolation and ITD

- GPLN members should provide feedback to the GLC on the accreditation checklists by July 31st for finalization. The documents can however be used during accreditation exercises starting from now.

4. Improvements in rRT-PCR methods

- GPLN endorses the use of commercial buffers (Quanta Tough Mix or Invitrogen Superscript III) for ITD and also endorses the implementation of the new ITD algorithm (for AFP and ES) including the quadriplex (panEV and multiplex Sabin 1.2 and 3), panPV, duplex WPV1 AFRO and SOAS genotypes, WPV3 WEAFB and WPV3 SOAS genotype assays.
- This new ITD algorithm using commercial buffers should be implemented during the 4th quarter 2014. GLC to work with the GSL in CDC to plan the roll-out.

5. Quality Assurance:

- WHO GLC and RLC need to develop a plan for identifying high risk cell banks to be tested at NIBSC by the cell authentication assay (from discussion of the small working group).
- Endorse the proposal for revised scoring of the ITD Proficiency Testing; Next PT panel will be a combination of both ITD testing and VDPV screening.

6. Biosafety and Biosecurity

- It is recommended that all regions complete the full Biorisk management training by the 2nd quarter 2015. Objective being to have at least one person trained in each polio laboratory.

7. Containment

- GPLN laboratories should serve as models and therefore destroy WPV whenever possible. In addition to containment of WPV, which has been under consideration for decades, attention must be paid to the implications of OPV2 withdrawal for containment. Rapid and comprehensive

detection of VDPV2 is a prerequisite for the switch from tOPV to bOPV. A procedure for destroying PV should be included in the Polio Laboratory Manual.

- Provide comments on GAP III by July 31st to WHO/HQ containment officer.

8. Environmental surveillance of PV

- Joint program and laboratory strategic planning will be required in order to expand ES. Significant expansion of ES led by the GPLN has occurred during 2013-2014 by the addition of several sites in Afghanistan, Nigeria, Pakistan and Kenya. Resources are needed before expansion so that the AFP surveillance-linked work is not compromised.
- Recommend that pilots be initiated soon, even for surveillance related to OPV withdrawal, in order to have functional ES when it is needed.
- It is recommended to revive the ES Working Group (comprising WHO and partners) that has been established, with the following responsibilities:
    - Establish a timeline for ES capacity building outlining resource needs for the expansion
    - Develop a plan and timeline for development and implementation of an accreditation system for laboratories performing concentration of sewage samples
    - Develop training plans
    - Develop plan for dealing with detections of PV by external (non-GPLN) laboratories
    - Develop an assessment tool for potential concentration laboratories and an assessment tool for potential environmental sampling sites, for inclusion in appendices of the ES Guidelines.
- GPLN endorses the two-phase (PEG dextran) as the WHO – supported method and also endorses proposed timeliness standards: concentration and VI in 21 days, shipment of isolates to a reference laboratory within 7 days if needed, 7 days for ITD testing, and 14 days for sequencing.
- Global and Regional Laboratory coordinators should work on the definition of a framework allowing implementation of priority actions identified during the SWOT analysis.
- Meeting participants are asked to (i) provide comments and feedback on the current version of the ES Guidelines by 31 July 2014 (including methods in the PLM rather than in the Guidelines should be considered) and (ii) provide comments on the ES Expansion Plan by July 15, 2014.