The 21st Informal Consultation on the Global Polio Laboratory Network

25-26 June 2015, WHO Headquarters, Geneva, Switzerland

- Final report of recommendations -

BACKGROUND INFORMATION

One of the main tasks of the WHO Global Polio Laboratory Network (GPLN) is to ensure that laboratory procedures and work practices are in line with the 2013-2018 Polio Eradication Endgame and Strategic Plan (PEESP) to better inform and orient the Global Polio Eradication Initiative (GPEI). Key objectives of the PEESP are (i) to detect and interrupt PV circulation, (ii) to strengthen immunization systems and support the withdrawal of OPV for immunization, (iii) to certify PV eradication and achieve PV containment and (iv) to plan the use of the vast experience developed by the GPEI as a legacy for other public health programmes to control, eliminate and/or eradicate infectious diseases.

It was noted this year that Global Polio Eradication Initiative is running directly under the WHO Director General Office (DGO) and Dr Hamid Jafari, WHO Director of Polio Operations and Research, reports to WHO DG.

The 21st Informal Consultation of the WHO Global Polio Laboratory Network (GPLN) was held in Geneva, Switzerland, on 25-26 June 2015. The meeting included participants from laboratories of the six WHO geographical regions including WHO Laboratory Coordinators. The main discussions focused on laboratory issues of relevance to the Global Polio Eradication Initiative (GPEI) and especially on current situation of poliovirus transmissions, expansion of environmental surveillance, diagnostic needs after withdrawal of Sabin 2 from trivalent OPV and Containment issues in relation with GAP III requirements.

A. GLOBAL OVERVIEW ON POLIO ERADICATION AND PEESP MID-TERM REPORT

Dr Hamid Jafari, the WHO Director of Polio Operations and Research, opened the meeting by thanking the GPLN for their excellent performance. In his talk on Mid-term review of the 2013-2018 PEESP he described the objectives defined by the Polio Eradication Endgame and Strategic Plan for years 2013-2018 (PEESP) and then reviewed the current state of the GPEI by highlighting considerable progress in Polio Eradication in the past year. He highlighted the fact that IPV has been used

successfully in campaigns in Kenya, Cameroon, Nigeria and Pakistan, overcoming numerous challenges. In addition, the polio "legacy in action" was demonstrated with rapid response to the Ebola outbreak in Nigeria. It was noted that Polio was declared a Public Health Emergency of International Concern.

A formal report of the Mid-term review will be published soon and shared with the Strategy Committee and the different stakeholders. In addition to comprehensive review of progress and lessons learnt the report also reveals recommendations to (1) increase surveillance capacity and quality (2) improve SIA quality, with a focus on missed children and intensified social mobilization (3) increase national and global capacity for outbreak preparation and aggressive response to both cVDPV and WPVs (4) rapidly accelerate support for Global Action Plan (GAP) (III) implementation.

The Global Polio Laboratory Coordinator gave an overview of the performance of the network and has shown that the GPLN has aligned its programme of work to meet PEESP objectives. He has highlighted the fact that GPLN was recognized as a "best practice in modern public health" by the Boston Consulting Group; "Critical success factors for GPLN include globally standardized approach, rapid and reliable case confirmation, frequent reporting, continuous training and linkages between national and international staff."

B. GLOBAL AND REGIONAL UPDATES ON WPV AND VDPV TRANSMISSIONS

The WHO Global and Regional Polio Laboratory Coordinators (GPLC and RPLC) 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 different surveillance activities.

Only one serotype of wild poliovirus (type 1 WPV) has been detected in the past 31 months. Wild poliovirus type 3 disappeared in November2012. The onset dates of the last AFP cases in Pakistan and Nigeria caused by type 3 WPV were 18 Apr 2012 and 10 Nov 2012, respectively. The last type 3 WPV positive sewage specimen was found in Nigeria 11 Nov 2012.The SEARO region was certified polio-free in March 2014. All WPV outbreaks have stopped, leaving endemic circulation in Pakistan and Afghanistan as the only source of wild polio circulation worldwide. Africa has been free of wild poliovirus since July 2014. Furthermore, recent outbreaks caused by cVDPVs were reported from South Sudan (cVDPV2), Nigeria (cVDPV2) and Madagascar (cVDPV1).

The 146 network laboratories have shown their capacity to adapt to changing situations in the GPEI. They are characterized by timely and accurate detection and reporting of WPV and VDPV, even in the absence of AFP cases. The laboratory performance has been very good despite challenges of increased workload and insecurity problems. Specifically Syria, Nigeria and Iraq National Polio Laboratories (NPLs) were mentioned since they are continuing to perform under dangerous security situation. In contrast, the laboratory in Donetsk, Ukraine cannot function fully at the moment. Altogether in 2014, 203,698 specimens were studied and more than 8500 poliovirus isolates characterized. Furthermore, 31 laboratories tested around 2900 sewage samples for poliovirus in 2014.

The Global Laboratory Coordinator also emphasized that in spite of all the efforts and achievements, there are recognized challenges in the GPLN (1) increasing workload and expectations

(2) staff attrition and competing priorities, (3) work loads faced by Laboratory coordinators continue to increase.

The Global and Regional coordinators, together with scientists from CDC and GSL, reported that important progress has been made in expansion of environmental surveillance (ES) in endemic regions. The reasons for the expansion are (1) to help identify any residual transmission in endemic and re-infected areas (2) to provide early indication of new poliovirus importation, (3) to detect rapidly any new emergence of VDPV and document the elimination of Sabin viruses following the withdrawal of OPV2 and eventual cessation of all OPV. They also highlighted that ES will be an important strategy to monitor the effectiveness of containment in facilities. In practise, this means a challenging time line since containment of type 2 poliovirus starts in 2016. The addition of ES to an existing polio laboratory cannot disrupt the laboratory's ability to complete its primary obligation to high quality AFP surveillance

The laboratories for expansion have been selected in three key regions (AFR, EMR, and SEAR) and establishment of activities and training are in progress. The expansion programme was started from the most critical countries/laboratories in EMR (Pakistan, Afghanistan) and AFR (Nigeria, Kenya, Senegal, Cameroon, South Africa) and they are ready to work while several others are procuring supplies to get ready for training and subsequent on site visits. According to the WHO Regional Coordinators, the most difficult challenge in the project seems to be delays in (i) buy-in by the national authorities, and (ii) procurements of supplies, reagents and equipment. Likewise, both Global and Regional Laboratory coordinators highlighted that there is an urgent need to clarify ownership for shared (intercountry) assets and infrastructure.

The document "Guidelines for Environmental Surveillance of Polio" has been completed (already available at the WHO website) and will be edited soon (for print). Altogether, three (inter-regional) workshops on ES have been organized. The protocol of the WHO recommended method for sewage concentration, 2-phase separation, was harmonized and users were trained. The next ES workshop in 2015 will be held in China.

Implementation of newly modified diagnostic methods within the GPLN is progressing. Following China, the "new" cell culture algorithm is being extended to the European region this year. Recently ITD testing sensitivity was increased 10 to 100-fold with the introduction of ITD version 4.0. For training on cell-culture, workshops were held in AFR (at NICD) in August 2014 (14 laboratories) and in WPR (China CDC) in December 2014 (39 participants). FTA Card implementation in all laboratories continues to be a priority for the GPLN. Furthermore, scientists from CDC and GSLs pointed out some key points in their talks:

1) New version of ITD (version 5.0) is under development and will come out within the next few months.
2) All cell banks from laboratories supplying cells to other laboratories should be authenticated. Likewise, cells from individual laboratories with possible problems should be tested. Technology transfer on cell-authentication rRT-PCR continues upon need.
3) Inclusion of PV2 in 2015 PT panels: Samples should be analyzed before April,1,2016.
4) No Sabin 2 will be included in 2016 Viral isolationPT panels.

5) In 2016, cell sensitivity testing must not include Sabin 2.
6) FTA card processing: to access the video for FTA Processing/ RNA Extraction, people will need to register to be a learner on the CDC TRAIN website. CDC TRAIN can be found at http://cdc.train.org, by clicking the CDC TRAIN icon from the CDC Learning Connection website at www.cdc.gov/learning, or you can click on the following link: https://cdc.train.org/DesktopModules/eLearning/CourseDetails/CourseDetailsForm.aspx?tabid=96&courseid=1048222

Presentations and discussions were also held on the progress of the development and evaluation of new diagnostic reagents and approaches. The scientist from GSL/Japan reported promising results on a direct detection of PV in stool and sewage samples using PV-particles with magnetic beads as concentration techniques. The scientist from NSL /Israel revealed their recent results on direct rRT-PCR detection on WPV type 1 from sewage. Scientists from GSLs emphasized that there is constant demand for better sensitivity and specificity. GPEI demands 100% sensitivity. As eradication progresses, increasing need for rapid turnaround is highlighted. Furthermore, discriminating components of complex virus mixtures in sewage specimens is challenging. Short term research needed for optimization of 2-phase separation (the WHO recommended method for sewage concentration) was presented and GPLN laboratories were invited to participate. The GPLC has presented an update on the GPLN management system which will help gather and streamline laboratory data for programmatic actions.

The legacy activities are currently a country- driven process. Four laboratories in pilot countries (India, Thailand, South Africa and Democratic Republic of Congo) were visited by the Consulting Group. Country governments commit to finalizing a transition plan by Q3 2016 using the GPEI transition guidelines. GPLN was a model for the rotavirus network in India. In Africa, GPLN has served as a model for rotavirus and measles virus networks. The polio programme directly affected the trajectory of Ebola in Nigeria.

C. PERFORMANCE IN PROFICIENCY TEST (PT) PANELS

As in previous years, careful reviews of the GPLN's quality assurance programme were presented by the 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 earlier, performance in 2014 has been excellent. 97.9% laboratories are fully accredited to perform the roles and functions required. Altogether, there are 94 ITD laboratories and 22 sequencing laboratories accredited. VP1 sequencing has been included in the QA programme for the past 3 years and improvements continue to be made.

D. SPECIFIC INFORMATION ON PT

1) RIVM will remain responsible for preparation of samples for proficiency test panels, distribution of panels and evaluation of isolation results. Sabin 2 will not be used anymore in PT panels.

   ITD; Many laboratories found the 2014 panel very challenging but 19 laboratories scored 100%. 98% of laboratories scored ≥90% after retesting and getting some guidance. Scientist from CDC

pointed out that there is a need for follow up and retraining, even in "experienced" laboratories (to eliminate complacency).

2) Sequencing; Laboratories that failed the 2014 Sequencing PT will receive troubleshooting and training. They have to repeat Sequencing PT and perform parallel testing of isolates. To provide a greater variety of sequences in the PT panels, CDC GSL is preparing additional noninfectious RNA templates for 2015 Sequencing PT. The panel is planned for autumn 2015. CDC team is also attempting to reduce the labor involved in PT evaluation and feedback by providing laboratories a checklist for submission of Sequencing PT results. They will also provide recommendations on software packages used for editing although there no requirement for specific software unless a PT is failed. Scoring system refinements are in progress, the aim is to move toward scoring consistent with the ITD and Virus Isolation PT.

E. GAP III AND CONTAINMENT

Containment of Polioviruses within GPLN laboratories is the highest current priority. In their presentation, the WHO Regional Coordinators also reported the current situation on containment. In most countries, WPV have already been destroyed and the present focus is on type 2 viruses. They concluded that the timeline to complete containment is very short. This will indeed be very challenging for endemic countries. Further challenges will come from other competing activities like the on-going expansion of ES. According to their experiences, (1) documentation process serves a critical role for compiling information that will be important for subsequent phases of certification (2) Laboratory survey and inventory process is effectively identifying laboratories with WPV materials (3) Strong political commitment towards laboratory containment of WPV activities is essential. They also reported that in spite of their efforts they have faced the following problems: (i) lack of support from some Ministries of Health, (ii) lack of legislation for laboratory registration (iii) no list of laboratories available at national level (iv) engaging with multisectoral laboratories, and (v) Limited capacity of containment coordinators for data management: entry, cleaning, analysis.

The Global coordinator concluded that in the Endgame the next critical steps are related to Biorisk Management (BRM) and GAP III / Containment. Training will be needed and GPLN human resources should be instrumental for this activity. For biosafety training, the 6 video modules are still available. A snowball approach to train laboratory staff on BRM principles and training on BRM/GAP-III implementation is ongoing. Training has been conducted in SEAR: Colombo March 2015 (15 PL and 10 Public Health Laboratories) and WPR: Manila May 2015 (13 PL, 1 RPLC invited). The GPLN targets to complete all regions (GPLN laboratories) by the end of 2015. During the last session, the participants of the meeting were divided into two groups and asked to discuss challenges on containment of polioviruses within GPLN laboratories.

Finally, five scientists of the GPLN who will/had retire(d) this year have received a recognition certificate from the Director of the Polio Programme for their positive inputs over decades. These retirees are Drs Jagadish Deshpande (India), Lucia Fiore (Italy), David Kilpatrick (USA), Lester Schulman (Israel), and Harrie Van der Avoort (Netherlands).

F. SUMMARY OF RECOMMENDATIONS:

1. **Changes in meetings schedule**

To accommodate the increased workload, align with the acceleration of polio endgame activities, and to improve the timing to implement recommendations from the Informal Consultation, the proposal to move the Polio IC from mid-year to the beginning of the year (end of January-early February) was adopted. The new format should be implemented by January 2016.

2. **Sequencing PT**
    a. Recommend refinement of the scoring algorithm as proposed, including switching to a subtractive algorithm.
    b. If a lab fails the Sequencing PT, then it will be required to submit edited files in a recommended software package in the repeat PT.
3. **VDPV reporting and classification**
    a. According to the current draft of the VDPV reporting and classification document, viruses that are genetically linked to a known cVDPV shall be classified as cVDPV.
    b. Viruses that are not genetically linked to a known cVDPV will be assigned the default category of "VDPV". After investigation, the virus will be assigned to a category: a, i, or c.
    c. Participants to the 21st IC are asked to review the VDPV reporting and classification document and send comments and feedback to WHO (diopo@who.int and tangermannr@who.int) by July 17th.
4. **QC/QA**
    a. Sabin 2 shall be removed from the Virus Isolation Proficiency Test for 2016 PT panels and from Cell Sensitivity Tests, starting 1st April 2016. No more Sabin 2 reference virus standards will be shipped from NIBSC from July 2015 and all Sabin 2 viruses stored in GPLN laboratories should be destroyed or contained following GAP-III requirements by 1st April 2016.
    b. A new test for the detection of Mycoplasma contamination in cell cultures using a real-time PCR format will be evaluated for introduction in network laboratories by end of 2015. Each Regional Laboratory Coordinator should designate (by the end of July 2015) one laboratory for pilot testing.
    c. RPLCs should document the authentication of cell banks in repository laboratories.
    d. Reviewers are encouraged to apply penalties when a laboratory fails to implement key recommendations made during previous accreditation reviews.

5. **Containment:**
    a. All Laboratories should be compliant with the containment phases as instructed by National Containment Committees and WHO Regional Office
    b. LCs to ensure that Laboratories, in consultation with National Authorities and WHO Regional Office, evaluate the requirements needed to become an essential or a non-

essential (diagnostic) facility, identify current gaps and devise a plan of action (by end of September 2015) to be able to comply with all requirements.

c. Recommend development and sharing with WHO/HQ of a regional dashboard to track the progress of containment activities in each region.
d. In collaboration with Regional offices, WHO/HQ should consider GAP-III translation in different WHO languages to ease implementation.

6. **rRT-PCR ITD:**
    a. Sub-optimal performance in ITD PT should be thoroughly followed up and corrective actions implemented including strengthening management, supervision and re-training laboratory staff
    b. ITD 4.0 to be optimized to correct minor anomalies and the roll-out plan for the new product communicated to WHO.
    c. ITD 5.0 to be designed to allow detection of any PV2 isolate following withdrawal of OPV2 in 2016.
7. **Polio Eradication Initiative/GPLN Legacy:**
    a. Environmental surveillance could be used to expand the search for other viruses/infectious agents to link with other programs. Enterovirus and Environmental Surveillance Guidelines were recently completed and have been posted on the WHO website.
    b. Implementation of Biorisk Management Systems in GPLN laboratories is a legacy that can be applied to other infectious agents.
    c. GPLN laboratories are encouraged to actively participate in legacy planning at the country level.
    d. Recommend adding a GPLN representative to the GPEI Legacy Management Group.
8. **Environmental surveillance:**

    Laboratories to communicate to the GPLC their willingness to participate in studies aiming to optimize testing algorithm and/or reduce ITD workload (please refer to presentation 5.5).