

# First consultation of the Regional Expert Panel for verification of Hepatitis B Control in the South-East Asia Region

New Delhi, India, 28–29 May 2019

## Background

Recognizing the public health burden, hepatitis B control has gained momentum in the WHO South-East Asia (SEA) Region over the past few years, especially through the following:

- ◉ Regional Action Plan for Viral Hepatitis 2016–2021 adopted by the WHO Regional Committee for South-East Asia.
- ◉ Regional Vaccine Action Plan 2016–2020 (RVAP) with the goal of accelerating hepatitis B control.
- ◉ Following other WHO Regions, the regional Immunization Technical Advisory Group (ITAG) recommended in 2016 that a regional control goal be established; with a target of  $\leq 1\%$  hepatitis B surface antigen (HBsAg) seroprevalence among children aged 5 years by 2020, and that this be aligned with the Global Health Sector Strategy on Viral Hepatitis 2016–2021 (GHSSVH).

To measure progress towards and verify the achievement of this goal, the WHO Regional Director for South-East Asia has appointed a Regional Expert Panel for Verification of Hepatitis B Control (SEA REP); with the following terms of reference:

- ◉ Conduct desk reviews of the information submitted by the countries for verification of the regional hepatitis B control goal as per protocol established in the “Guidelines for verification of achievement of hepatitis B control target through immunization in the South-East Asia Region” prepared by the Regional Office.

- ◉ Execute visits to countries and WHO offices where be necessary.
- ◉ Participate in technical meetings organized by the Regional Office as required.
- ◉ Make recommendations to the Regional Director on whether the target of reducing chronic hepatitis B prevalence to less than 1% among children at least 5 years old has been achieved.

## Objectives and participants

The first consultation of the SEA REP was held in New Delhi, India, on 28–29 May 2019. The objectives of the consultation were to:

- ◉ provide the current status/overview of the global and regional situation of hepatitis B control;
- ◉ discuss and finalize the draft “Guidelines for verification of achievement of hepatitis B control target through immunization in the WHO South-East Asia Region”; and
- ◉ finalize a verification workplan and timeline for verifying status of the hepatitis B control target in the WHO South-East Asia Region.

The consultation was attended by five of the eight panel members, two members participated remotely through virtual communication, and was supported by a WHO Secretariat.

## Opening

The consultation was opened by Dr Neena Raina, Director a.i. of the Department of Family Health,

Gender and Life Course. She welcomed participants on behalf of the Regional Director, Dr Poonam Khetrpal Singh, who was unable to attend due to prior commitments. Dr Raina conveyed the welcome message of the Regional Director, in which she expressed her satisfaction about the Region's progress in combating vaccine-preventable diseases (VPD). It was noted that the Region was certified polio-free in 2014 and was validated in 2016 to have eliminated maternal and neonatal tetanus as a public health problem. In addition, four countries of the Region have now been verified for having eliminated indigenous measles, and six have been verified for having controlled rubella and congenital rubella syndrome.

Dr Poonam Singh at the same time emphasized that despite notable progress in accelerating disease control efforts, viral hepatitis continues to be a major problem. Every year, viral hepatitis is estimated to be responsible for almost 300 000 deaths across the Region, which is more than that due to HIV and tuberculosis combined. An estimated 39 million people live with chronic hepatitis B in the Region, and an estimated 10 million live with chronic hepatitis C. Together, hepatitis B and C account for around 90% of hepatitis-related mortality.

The most effective way to stop this, the Regional Director said, is through universal vaccination of all newborns and infants. Since Member States began vaccination against hepatitis B in early infancy, chronic infections have increasingly been prevented, thereby averting life-threatening complications. Point-of-care diagnostics and laboratory testing, as well as effective treatment, are also now available and hold substantial promise, especially given the unprecedented progress in reduction of costs and access to the newer, directly-acting antiviral drugs. The Regional Director noted that the South-East Asia Region's Regional Action Plan for Hepatitis, which aims to end viral hepatitis as a public health threat by 2030, will help take advantage of these breakthroughs.

Dr Poonam Singh informed that in order to foster collaboration and coordination across different programmes and divisions – especially in view of the diversity of control strategies that must be

implemented – an internal working group has been established with members from the immunization, hepatitis control, maternal, neonatal and adolescent health teams. The working group will also help harmonize advocacy strategies and create a platform to find solutions to the current challenges.

Most people living with hepatitis B are asymptomatic, the Regional Director said. Since these chronic infections are rarely apparent, especially in childhood, surveys that collect and test blood specimens are required to estimate the number of infected persons. Measuring these seroprevalence rates among vaccinated cohorts is critical for monitoring the impact of hepatitis B vaccination. Dr Poonam Singh welcomed the fact that several Member States in the Region are collecting seroprevalence data to more accurately determine the current burden of disease among children, as well as to measure progress towards the 2020 goal.

The Regional Director said that verification of control of hepatitis B is the goal. Once a Member State has conducted an internal evaluation and is confident that the target has been reached, a verification data package and supporting documents can be submitted to the Regional Office. It is then the task of the SEA REP to perform a detailed desk review of the data submitted in the verification package and examine the evidence provided as per the criteria and indicators set out in the "Guidelines for verification of achievement of hepatitis B control targets through immunization in the WHO South-East Asia Region".

Once a consensus has been reached on a country reaching the target, the Regional Director is provided with a report, following which an official letter is sent to inform the country about the verification decision. Reports are also sent to the ITAG and the WHO Regional Committee.

The Regional Director in her address also acknowledged that the task at hand is very significant. She expressed her gratitude to the new SEA REP members for their efforts to address one of the pressing public health problems of South-East Asia.

## Global and regional overview of viral hepatitis control

Dr Bharat Rewari, Scientist, HIV/Hepatitis, Department of Communicable Diseases, WHO Regional Office, presented a global and regional overview of viral hepatitis control.

The World Health Assembly in 2016 endorsed the GHSSVH that calls for the elimination of viral hepatitis and entails a 30% reduction in incidence and 10% reduction in mortality by 2020 and 90% reduction in incidence and 65% reduction in mortality by 2030. However, in 2015, only 9% of the estimated 257 million people with hepatitis B were diagnosed, of which only 1.7 million are on treatment. Yet, 1.1 million people were newly infected in 2017.

Modelling showed that the following five core interventions with sufficient coverage would lead to the elimination targets being realised:

- three doses of hepatitis B vaccine (HepB),
- prevention of mother-to-child transmission (PMTCT) of hepatitis B through a HepB birth dose, ideally given within 24 hours (HepB BD),
- blood and injection safety,
- harm reduction for people who inject drugs (PWID), and
- timely diagnosis and treatment of hepatitis B.

Globally, coverage of the third dose of HepB (HepB3) was 84% in 2017 while the HepB BD coverage was at 39%. Immunization and injection safety are on track with some gaps against the 2030 targets but coverage of other interventions, especially among PWID and on the diagnosis and treatment front, are either incomplete with major actions required or have made little progress. For blood safety, 97% of countries that report to WHO now screen all blood donations for transfusion-transmitted infections. Health-care injection safety, however, remains an issue. Comprehensive harm reduction services are far from the target with little progress noted. The treatment coverage for hepatitis B has increased from 1.7 million in 2015 to 4.5 million in 2016.

In the 11 countries of the SEA Region hepatitis B prevalence ranges from 0.9 to 7.1 with over 39 million estimated to be living with chronic hepatitis B. One country has already adopted a national plan for viral hepatitis, while it is in advanced stages of development in another four countries. The number of syringes distributed per PWID ranges between 25 to 243 in countries of the Region, whereas the regional target for 2020 is 200. Medicines for the treatment of hepatitis B are available in eight countries with an annual cost ranging from US\$ 72 to US\$ 646 though WHO has negotiated a price of US\$ 30 per year. Prevalence of chronic hepatitis B among children under 5 years of age in 2017 is estimated (based on modelling) at 0.26 %, whereas it was estimated at 0.8% globally (with a global target for 2020 of equal or less than 1%).

The Regional Action Plan for Viral Hepatitis 2016–2021 recommends five key strategies for controlling the epidemic and care of those already infected with hepatitis:

- All infants and newborns must be immunized at birth for hepatitis B virus (HBV), with an additional two to three doses.
- Injection safety in health settings must be ensured, including the use of reuse prevention syringes.
- Blood safety must also be assured by ensuring that every unit of blood and related products is screened for hepatitis A and C.
- Drinking water must be made safe, and all people should have access to effective sanitation.
- Diagnostic and treatment facilities for hepatitis B and C should be immediately scaled up.

### Key challenges include the following:

- The burden of disease is still not known in many countries.
- The largely asymptomatic nature of the disease with low levels of awareness among the general population, as well as those at risk impedes early diagnosis and treatment.
- While HepB3 coverage has improved, HepB BD coverage is still to catch up.

- ◉ Harm reduction interventions that are key to address the epidemic among PWID are lagging behind; countries with large PWID populations are only providing 27 needles per year.
- ◉ Governance issues, particularly with multisectoral coordination such as with immunization, blood safety and harm reduction, continue to be challenging.

## Hepatitis B control through immunization: regional update

Dr Sigrun Roesel, Technical Officer, VPD, Immunization and Vaccine Development Unit (IVD) at the Regional Office, presented the regional situation from an immunization perspective. In 2018, all 11 countries in the SEA Region continued to have HepB in their routine immunization schedules as part of combination vaccines, and eight countries (Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Thailand and Timor-Leste) had a universal HepB BD (WHO Monitoring System 2018).

The overall HepB3 in the Region increased from 54% in 2010 to 88% in 2017 (source: WUENIC). As per the draft WHO-UNICEF best estimates in 2018, HepB3 coverage was reported to be  $\geq 90\%$  in eight countries (Bangladesh, Bhutan, Democratic People's Republic of Korea, Maldives, Myanmar, Nepal, Sri Lanka and Thailand), while India reported 89%, Indonesia 79% and Timor-Leste 83%. Among the eight countries that included HepB BD in their vaccination schedule in 2018, coverage was  $>90\%$  in four (Bhutan, Democratic People's Republic of Korea, Maldives and Thailand). India and Indonesia reported 54% and Myanmar and Timor-Leste – where the HepB BD was introduced in 2016 – reported 14% and 61% respectively. Several countries have sustained high HepB BD and HepB3 coverage for at least five years and have in all likelihood achieved the target of reducing chronic hepatitis B prevalence to less than 1% among children.

National sero surveys among children at least 5 years of age are available in Bangladesh, Bhutan, Nepal and Thailand and indicate low post-vaccination infection rates in the surveyed cohorts. Maldives is

implementing a national school-based survey among Grade 1 children and Democratic People's Republic of Korea is planning to conduct a national household-based survey among children aged over 5 years.

## Cross-cutting aspects and coordination with maternal and reproductive health and child and adolescent health programmes

The joint presentation by Dr Chandani Anoma Jayathilaka, Medical Officer, Maternal and Reproductive and Health, and Dr Rajesh Mehta, Regional Adviser, Child and Adolescent Health, explored the interventions to support hepatitis B control that can be delivered in reproductive, maternal, neonatal and child health (RMNCH) packages. These include:

- ◉ early antenatal care (ANC) and screening;
- ◉ rapid diagnosis and timely and appropriate treatment in pregnancy as well as during and after childbirth, partner testing and treatment;
- ◉ universal precautions to prevent transmission during intrapartum care;
- ◉ immunization of neonates and infants against hepatitis B, including a timely birth dose (HepB BD);
- ◉ if available, hepatitis B immune globulin (HBIG) given within 12 hours of birth to infants whose mothers are known to be HBsAg-positive or whose HBsAg status is unknown; and
- ◉ preventing unintended pregnancies.

The Global Strategy for Women's Children's and Adolescents' Health (2016–2030) calls for screening for and prevention and management of sexually transmitted infections (syphilis and hepatitis B) while the WHO guidelines on hepatitis B and C testing recommend that in settings with a  $\geq 2\%$  or  $\geq 5\%$  HBsAg seroprevalence in the general population, HBsAg serological testing be routinely offered to all pregnant women in antenatal clinics, with linkage to prevention, care and treatment services. Couples and partners in antenatal care settings should be offered HBV testing services.



The Regional Action Plan for Viral Hepatitis 2016–2021 includes a target of 75% of pregnant women screened for hepatitis B and post-exposure prophylaxis provided to exposed newborns in Member States implementing such policies. However, no ANC screening of pregnant women for hepatitis B is included in the 2016 WHO recommendations on ANC for a positive pregnancy experience.

In terms of immunization, the WHO recommendations on newborn health also emphasize that all infants should receive their first dose of HepB as soon as possible after birth, preferably within 24 hours. This is crucial in areas of high hepatitis B endemicity, but important even in intermediate and low-endemicity areas. This is rated as strong recommendation, with moderate quality evidence.

While ANC is a vehicle for multiple interventions and linking programmes, data on the prevalence of HBsAg among pregnant women are currently very limited in the SEA Region; while data are urgently needed for advocacy. ANC coverage has increased over the years but not reached the 90% target. Nearly one in three women across the Region still does not get even one ANC visit (the regional average is 77%). Although coverage has increased in the last decade, four ANC visits remain low at 56% in the Region.

Data indicate that almost all women attending ANC have their blood pressure measured. However, in countries with low ANC coverage though it is important to monitor high risk mothers, urine and blood samples are collected less frequently. In addition to specific service delivery challenges, availability of trained health staff remains an issue and in 9 out of 11 countries of the Region the density of health workers is lower than the levels recommended in the WHO Global Strategy on Human Resources for Health.

The ways forward include the following steps and interventions:

- ⦿ Increasing institutional deliveries and skilled birth attendance.
- ⦿ Including HepB BD in essential newborn and post-natal care packages and ensuring compliance

through supervision and quality improvement approaches.

- ⦿ Integration and coordination instead of vertical programmes (EPI, EMTCT and RMNCH).
- ⦿ Integrated service delivery models (MCH clinics provide vaccines / newborn care packages deliver HepB BD).
- ⦿ Joint monitoring and evaluation of programmes.
- ⦿ Strengthening logistics and the health workforce for integrated service delivery; with improved availability of vaccine in the labour and postnatal ward, and MCH workers in delivery/post-natal wards proving vaccination.
- ⦿ Addressing health finance aspects in terms of user fees, essential service packages, cost of screening tests and developing cost-sharing models.
- ⦿ In addition to having clear policies and updated guidelines for ANC, encouraging countries to include ANC in the universal health coverage package.

## ITAG recommendations

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Dr Sunil Bahl, Team Leader of the IVD Unit at the Regional Office, summarized the historical perspective of hepatitis B immunization in the SEA Region and recent ITAG recommendations. Prior to 1999, only four SEA Region countries had introduced HepB in their routine national immunization programmes (Bhutan, Indonesia, Maldives and Thailand). Five more countries integrated HepB into their national immunization programmes in 2003, with support from Gavi, the Vaccine Alliance (Bangladesh, Democratic People's Republic of Korea, Myanmar, Nepal and Sri Lanka). India initiated a pilot project in 33 districts and 15 cities which was gradually expanded to nationwide use by 2011. Timor-Leste introduced HepB3 in 2007. Gavi supported Indonesia to introduce HepB BD as HepB-Uniject – a pre-filled, non-reuse injection device.

A status review in 2007 had recommended that the SEA Region should set the hepatitis B control target using the HBsAg prevalence rate in the general population as proxy for reduction of chronic

disease and death. Measurement of vaccine impact should be an integral part of HepB introduction, wherever feasible, and while the HepB BD may not be a priority for all, countries should consider it depending on the stage of their programme and disease control targets. Studies to determine the role of perinatal transmission and the feasibility of adding the HepB BD should be supported.

A comprehensive literature review, conducted with support from a team of the Accelerated Disease Control and VPD Surveillance Branch of the Global Immunization Division at the US Centers for Disease Control and Prevention (US CDC) in 2015, estimated the overall intermediate endemicity of chronic hepatitis B infection at 3%–5% but with prevalence variable by country. It also concluded that a SEA regional goal of HBsAg $\leq$ 1% in children 5 years of age in 2020 could be achieved with political will, sufficient resources and adequate preventive strategies. This would put the Region in line with other regional control goals which have been established as follows:

- Western Pacific Region: HBsAg $\leq$ 2% among 5-year-old children in 2012 and  $\leq$ 1% in 2017
- Eastern Mediterranean Region:  $\leq$ 1% in 2015
- African Region: <2% in 2020
- European Region:  $\leq$ 0.5% among vaccinated birth cohorts in all countries by 2020.

Subsequently the ITAG recommended in 2016 that countries should undertake systematic reviews of HepB coverage, identify gaps and causes of under-immunization, especially with regard to the HepB BD, and develop/implement strategies to bring coverage to target levels. Activities required for achieving HepB coverage goals should be reflected in the national comprehensive multi-year plans (cMYP) or other EPI plans. Hepatitis B immunization strategies should also be reflected in national action plans for the control of viral hepatitis. The national immunization technical advisory groups advocate and oversee the coordination between departments to achieve the immunization goals.

The ITAG also recommended to the Regional Office to establish a regional goal for the control of hepatitis B as part of the RVAP 2016–2020.

This regional control goal should be in alignment with the GHSSVH, i.e. a target of  $\leq$ 1% HBsAg seroprevalence among children aged 5 years, by 2020. Subsequently, an action plan for accelerating hepatitis B immunization towards the regional control goal should be developed and aligned with the RVAP.

In 2017, the ITAG stated that the recommendations made at the 2016 meeting remained valid but additionally countries without HepB BD should assess whether introduction is a relevant strategy based on their epidemiological situation. Countries providing a HepB BD should conduct assessments to identify causes for low coverage, particularly for health facility births. The Regional Office should support countries in measuring the impact of control measures taken by conducting nationally representative HepB sero surveys among children. This will also help document progress towards the 2020 target. The Regional Office should also consider a verification framework with pilot application in selected countries which have demonstrated evidence of having achieved the 2020 control target.

In 2018, the ITAG stated that recommendations made at the 2017 meeting remain valid, while additionally the proposed verification process should be finalized with implementation initiated prior to the next (2019) ITAG meeting. National programmes should prioritize achieving high coverage of HepB3 and ensure that children <5 years of age are covered with catch-up/patch-up vaccination with HepB3. Countries should introduce a HepB BD and ensure timely delivery where indicated by disease epidemiology. Countries with a high percentage of home deliveries should explore the feasibility of introducing HepB using Uniject.

## Overview of other VPD control verification structures

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### Certification of polio-free status

Dr Supamit Chunsuttiwat, Chairperson of the South-East Asia Regional Certification Commission for Polio Eradication (RCCPE) (2012–2018), summarized the certification process. In 1988 the World Health Assembly passed a resolution to eradicate polio

globally. A formal process for the certification of polio eradication was established on the basis of the experience gained during smallpox eradication. Independent groups of experts were designated at global, regional and country levels to set criteria and conduct the certification process with a three-tiered approach. Certification of polio eradication is conducted on a regional basis and each region can consider certification only when all countries in the area demonstrate the absence of wild poliovirus transmission for at least three consecutive years in the presence of certification standard surveillance.

A Global Commission for the Certification of the Eradication of Poliomyelitis (GCC) was appointed by the Director-General of WHO in 1995 to oversee polio eradication certification activities at the global level. The GCC, at its first meeting, established basic definitions, principles and criteria upon which certification would be based, and defined the terms of reference and operating procedures of certification bodies at regional and country levels. Regional Certification Commissions (RCCs) were then established and started functioning in WHO regions: 1995 in the Eastern Mediterranean Region, 1996 in Europe and the Western Pacific, 1997 in South-East Asia and in the African Region in 1998.

The WHO Director-General in 1995 charged the GCC with the main tasks of defining the parameters and processes by which polio eradication will be certified, guiding regions and countries in establishing their data collection processes; receiving and reviewing the final reports of RCCs of polio eradication; and issuing, if and when appropriate, a final report to the Director-General certifying that global polio eradication had been achieved.

RCCs are appointed by the Regional Directors of each WHO Region and include members of the GCC who are from the Region (who is usually appointed as the RCC chairperson) as well as representatives of other WHO regions. After a three-year period of freedom from indigenous wild poliovirus transmission under conditions of certification-quality surveillance, and considering all necessary evidence, including the views of National Certification Committees (NCCs) and results of field visits to countries, RCCs have the authority to certify the eradication of indigenous wild poliovirus in a region.

NCCs are responsible for assessing and verifying national documentation on polio-free status, collected and provided by the secretariat of the national ministry of health, prior and post certification. NCCs cannot certify polio eradication in their own country, but present their opinion, with supporting documentation, for assessment by the RCC. The GCC stated that members of both RCCs and NCCs should be independent leading experts in relevant disciplines such as public health, epidemiology, virology and clinical medicine.

The International Certification Commission for Polio Eradication (ICCPE) in the South-East Asia Region was established in 1997. National Certification Committees for Polio Eradication (NCCPEs) had been established by the end of 1998. From 1997 to 2006, the ICCPE held eight meetings and accepted national documentation for polio-free certification and phase 1 laboratory containment from nine countries: Bhutan, Bangladesh, Democratic People's Republic of Korea, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka and Thailand.

In 2008 the ICCPE was renamed as SEA-RCCPE. In January 2012, the SEA-RCCPE at its second meeting decided to intensify activities beyond its annual meeting, based on the progress made in India and the need to accelerate activities. Over the next 14 months, the SEA-RCCPE met four times, with two main objectives: to ensure that the polio-free certification and phase 1 laboratory containment documents of the nine countries that have already been accepted were updated; and to support the submission of the full documentation from the two remaining countries, India and Timor-Leste. As part of their intensified activities, RCCPE also provided support to the NCCPEs with advocacy and review missions to each country in 2013.

Since regional certification of polio-free status on 27 March 2014, the terms of reference of the RCCPEs were updated, and member tenures extended and synchronized with the Global Polio Eradication Initiative's Endgame Strategic Plan 2013–2018. NCCPEs were requested to stay active, with updated terms of reference, at least until global certification to support countries to remain polio-free, maintain preparedness for poliovirus importation and meet polio endgame requirements. Some NCCPEs now

also serve as the measles elimination verification committee which requires wide range of expertise, a strong role in advocacy and participation in various activities.

### **Validation of maternal and neonatal tetanus elimination (MNTE)**

Dr Sigrun Roesel summarized the MNTE validation process led by WHO in collaboration with UNICEF and the respective ministries of health. The criteria for elimination of neonatal tetanus (NT) as a public health problem is defined as having less than one NT case per 1000 live births in every district or similar administrative unit in the country each year. Maternal tetanus is assumed to be eliminated once NT elimination has been achieved. Validation of MNTE is recommended once countries complete the implementation of all planned MNTE activities using the high-risk approach and claim that they have achieved MNTE. The validation process consists of several components:

- ◉ *Review of district level data* (on NT surveillance, tetanus toxoid (TT) immunization and MCH services): The data used are a series of core indicators (reported NT cases, TT2+, results of TT supplementary immunization activities, clean delivery coverage), complemented by additional indicators which can be country-specific (DTP3, ANC attendance, urban/rural status, vacancy levels among health staff, women's literacy, etc). When recent relevant survey data are available, they are also used. The objective of the systematic district-level data review is to assess if elimination appears to have been achieved, and to identify districts with weakest performance.
- ◉ *Field visit*: When the data review alone does not permit a conclusion on elimination status, field visits to districts with weak performance may be required. A field visit typically includes evaluation of health facilities where records are reviewed and health workers, community leaders and women are interviewed. Such field visits yield useful information on the performance of the health system, access to care and neonatal care, challenges to service delivery, skill attendance at birth, application of substances to umbilical cord and interactions of the health system with the

community. An associated rapid convenience survey gives some useful information on coverage for a number of immunization and reproductive health indicators.

- ◉ *Validation survey*: An MNTE validation survey is conducted if the level of risk for MNT is found to be very low in all districts but a decision still cannot be reached about the MNTE status of a country following the district data review (and field visits, when performed). The recommended community-based neonatal mortality survey method uses a combination of a lot quality assurance (LQA) and cluster sampling (CS) survey methodologies to judge whether the neonatal tetanus mortality rate is probably greater than 1 NT death/1000 live births in the selected survey district (elimination not achieved) or not (elimination achieved). The LQA-CS survey is carried out in the district(s) found to be the most poorly performing in the country with regard to MNTE. The logic is that if NT elimination can be validated in the weakest district(s), elimination can be assumed in the better performing districts and, therefore, in the country or geographical entity being validated as a whole.
- ◉ *Long-term plan for sustaining MNTE*: If elimination has been achieved, strategies need to be adjusted to sustain the progress. These can include, but are not limited to, the administration of booster doses of tetanus toxoid-containing vaccines (TTCV), including through schools, and/or immunization of new cohorts of women of reproductive age with TTCV, increasing access to skilled attendants at birth, and clean cord care practices and NT surveillance. Plans for sustaining MNTE should be included in the cMYP for immunization.

### **Verification of measles elimination and rubella/congenital rubella syndrome control (CRS)**

Dr Sunil Bahl presented the principles and processes followed by the South-East Asia Regional Verification Commission (RVC). This includes its functions as an independent commission involving two levels of external and independent expert bodies in the verification process – besides the RVC there are national verification committees (NVCs). The RVC



verifies independently for countries and eventually for the Region and applies standard procedures and criteria (based on a well-defined framework with lines of evidence and criteria for verification). For larger countries the RVC verifies by the second-level administrative unit when appropriate. It also utilizes the opportunity to document the impact the initiative has on strengthening the health system.

In its normative function, the RVC reviews and establishes criteria and procedures, including a plan of action for monitoring progress and verifying the achievements. Its verification function entails that the achievement and maintenance of measles and rubella elimination or control for individual countries and the Region is verified. It also monitors progress toward measles and rubella elimination or control and in its post-verification role ensures that the achievements are sustained.

The advisory function of the RVC guides NVCs on verification criteria, requirements and annual reporting procedures, reviews and analyses the annual reports submitted by NVC committees, provides feedback and conducts field visits when needed to monitor progress and verify evidence, and provides guidance to the governments. Additionally, advocacy functions are extended at the subnational, national and regional levels. The RVC chairperson is responsible for leadership and management functions to define internal processes, coordinate review processes and report to the Regional Director.

In terms of the operating process, the framework for verification of measles elimination and rubella/CRS control and an annual reporting template are shared with all NVCs through the respective WHO country offices months before the meeting. Reports received from all 11 Member States of the Region are shared with the RVC members electronically for review. Two RVC members are assigned as reviewers to each country report submitted by NVCs while the Regional Office also independently reviews each of these reports. Reviewer comments are shared with countries through the respective WHO country offices at least 15 days before the meeting. Field visits by selected members are conducted in countries based on the country report and with a focus on countries close to elimination.

## **Guidelines on verification of achievement of hepatitis B control targets through immunization in the South-East Asia Region**

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Dr Sigrun Roesel reiterated that the draft guidelines provide overall guidance on verifying a country's achievements vis-à-vis the hepatitis B control target through immunization. Data and indicators to be used for verification and the verification procedures are described in the guidelines as well as the actual process to be followed. They also contain various tools to support the verification process.

The verification guidelines include, as main evidence needed for verification, the prevalence of chronic hepatitis B among vaccinated cohorts and sustained high immunization coverage; to be demonstrated by the following means:

- ◉ HBsAg prevalence among children: at least one source of nationally representative data among children 5 years or older born after the nationwide implementation of universal hepatitis B infant immunization.
- ◉ HepB BD and HepB3 at national and subnational levels: for at least 5 years with coverage levels in line with the RVAP targets.
- ◉ If other sources of data, such as antenatal HBV screening, are available they may be included as supplemental information to help the SEA REP with its decisions.

The guidelines describe the criteria for a valid HBsAg serosurvey for the purpose of verification in terms of representativeness, precision, age group, sero markers, ethical standards and quality assurance of laboratory procedures.

To begin the verification process, the country submits a formal request with the completed verification data package and supporting documents to the Regional Office. A verification team is then established comprising three SEA REP members to perform a detailed desk-review of the data submitted in the verification package. The verification team will examine evidence in each country on a case-by-case basis following the criteria and indicators in the guidelines.

Some criteria may be adjusted by the panel, considering the country's context, for example, subnational variations of hepatitis B epidemiology, other interventions to reduce the risk of HBV infection, and demographic characteristics. The review team may take additional information into consideration, including from its own literature review. The verification team will reach its conclusion by consensus and present them to the SEA REP for a final consensual decision by all panel members. Following this a report will be submitted to the Regional Director detailing whether the country has reached the target of reducing chronic hepatitis B prevalence among children to  $\leq 1\%$ , with reasons for the findings.

### Documenting impact: countries with recent or planned serosurveys and relevant lessons

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The presentation of Dr Rania Tohme, SEA REP member, provided an overview of the various methods that could be used to assess the impact of hepatitis B vaccination on disease burden and summarized the methodological aspects of hepatitis B serosurveys with some country examples. Approaches for measuring impact include surveillance, monitoring disease outcome (hepatocellular carcinoma/HCC) and establishing the prevalence of chronic hepatitis B infection (serologic survey).

In terms of surveillance, VPDs like polio, measles or rubella allow testing for clinical symptoms to estimate of burden of disease, progress towards regional goals and evaluate service delivery of immunization. In the case of hepatitis B >99% children are asymptomatic, not allowing for quality surveillance. As the disease resulting from HBV infection is seen more than 25 to 50 years after, it is not possible to evaluate the performance of immunization in a timely manner.

HCC is rare in children and more common in older adults. As the infection may take 50–60 years to progress to cancer, the impact of vaccination is not seen for a long time. Evaluation and diagnosis of HCC needs access to advanced medical care and

reporting of HCC requires robust cancer registries with high-quality data.

The most common survey methods are population-based cluster surveys and classification surveys, and these require five essential steps to design the survey. Defining objectives may include establishing chronic HBV seroprevalence in terms of verifying achievement of a set goal, assessing progress towards the goal, understanding risk factors for hepatitis B infection and measuring impact of vaccination by assessing pre- versus post-vaccination cohorts as well as advising the immunization programme if the HepB BD is needed. Frequently selection of the survey approach will be based on a combination of time and resources availability.

Planning the survey needs to identify age groups for which the history of the vaccination programme, vaccination coverage achieved, and objectives of the survey will guide the age group chosen. The study must be representative of the entire population for verification purposes and thus include migrant populations, remote/hard-to-reach areas, expatriates, etc. Convenience samples such as from blood banks, clinic/hospital specimens or volunteers at a central site are not acceptable. These can be used as supporting evidence but cannot be the primary evidence for the achievement of the goal.

In terms of sampling and sample size most countries should do a 2–3-stage cluster sample, based on the geographical size of the country. Larger countries that are harder to get around are usually covered as 3 stages for logistical reasons. Further decisions need to be made on whether to choose villages or schools.

If the approach is house-to-house it involves searching for children in the selected age group; if the survey is school-based all children in one grade in the selected school will be included. The sample size depends on the expected seroprevalence.

As a last step in the survey planning it has to be decided which methods are to be used for blood collection (serum or finger prick) and testing; usually sensitivity  $\geq 95\%$  and specificity  $\geq 95\%$  are required and tests should be approved by national regulatory

authorities or prequalified by WHO. The selection of hepatitis B biomarkers of interest needs to be made (HBsAg is usually enough in children) and decisions taken if testing for other VPDs or other diseases of interest to the country should be included.

Examples of surveys where hepatitis B testing can be added include but are not limited to Demographic Health Surveys, Multiple Indicator Cluster Surveys, vaccine coverage HIV/AIDS and malaria serosurveys. Consideration needs to be given to requirements of rapid tests or blood collection if not part of the protocol and adding children within the targeted age group if not already included. Integration with other surveys provides the opportunity to test for other VPDs in children (measles, rubella, tetanus, diphtheria) and can save costs. HBsAg rapid tests are easy to use in a study setting and the study team can share test results with the family immediately and the use of multibead assay allows to test for several VPDs and neglected tropical diseases using few dried blood spots.

Classification surveys may be used if seroprevalence is very likely below or above the target (null) threshold, require smaller sample sizes than surveys calculating precise estimate, are less costly and require a minimum of 15 clusters in each stratum. They may combine data from the lowest levels to *estimate* coverage at the higher levels and estimates at the aggregated levels are often quite precise. They may though not yield a precise quantitative estimate of coverage at the lowest geographical level (districts or provinces). This type of survey can be used to assess pockets of high infection in countries that have achieved the target to guide prevention interventions.

## Key discussion points

### Key discussion points of the consultation included the following:

- ⦿ Definition of control as immunization is the key but not the only prevention/control strategy.
  - Control goal has been established by the SEAR ITAG and is in line with the GHSSVH

impact target of 30% incidence reduction by 2020.

- It should be noted that the GHSSVH also monitors programme and process targets.

- ⦿ Essential criteria for verification and use of additional information if supplementary activities are implemented.
- ⦿ Immunization coverage data quality and the WHO and UNICEF annual process of collecting information through a standard questionnaire (the Joint Reporting Form) and applying a (documented) stringent review for completeness and consistency.
  - Need for subnational data for verification to identify underserved and high-risk populations, also affected by inward and outward migration and potential source of HBV infection.
- ⦿ Serosurvey aspects, in terms of:
  - confidence interval and precision (in the context of point estimate),
  - need for data stratification in countries with large populations,
  - realistic sample sizes in conditions of limited resources, and
  - validation of test kits.
- ⦿ Verification procedure in terms of
  - SEA REP members taken additional information into consideration such as unpublished reports, surveys, literature review and calling upon specific experts,
  - final conclusion on achievement of control goal by the entire SEA REP,
  - meeting as and when required (also through electronic means),
  - chairpersonship,
  - role of the WHO SEARO Secretariat and
  - future needs for reconsideration and modifications of the current guidelines based on developments in hepatitis B control.
- ⦿ Classifications in the tool for evaluating country verification data and outline of reference points
  - Some criteria can only either be acceptable or not acceptable.

## Workplan and timelines (tentative)

Sr	Activity		
1	Sharing outcomes of 1st consultation with WHO country offices	30 May 2019	IVD
2	Planning discussions with Bangladesh, Bhutan, Nepal and Thailand	30 May	IVD
3	SEA ERP consultation posted on IVD website	30 May	IVD
4	Final draft verification guidelines to REP members	3 June	IVD
5	Comments on final draft guidelines	3–9 June	SEA REP members, participants 1st consultation
6	SEA REP section on IVD website	3 June	IVD
7	Draft report of 1st consultation to REP members	5 June	IVD
8	Comments on draft consultation report	5–11 June	SEA REP members, participants 1st consultation
9	Final verification guidelines	10 June	IVD
10	Quarterly meeting of SEARO informal hepatitis B working group	Week of 10 June	IVD, CAH, MRH, CDS
11	Final report of 1st consultation	13 June	IVD
12	Country data review	11–21 June	SEA REP members
13	2nd face-to-face consultation of REP	25–26 June	SEA REP members, WHO Secretariat
14	REP consultation and country data review outcomes presented to ITAG meeting	Week of 11 July	IVD