THIRD STRATEGIC AND TECHNICAL ADVISORY COMMITTEE FOR VIRAL HEPATITIS AND SIXTH HEPATITIS B IMMUNIZATION EXPERT RESOURCE PANEL JOINT CONSULTATION

17–20 September 2018
Manila, Philippines
Third Strategic and Technical Advisory Committee for Viral Hepatitis and Sixth Hepatitis B Immunization Expert Resource Panel Joint Consultation
17–20 September 2018
Manila, Philippines
MEETING REPORT

THIRD STRATEGIC AND TECHNICAL ADVISORY COMMITTEE (STAC)
FOR
VIRAL HEPATITIS

Convened by:

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR THE WESTERN PACIFIC

Manila, Philippines
17-20 September 2018

Not for sale

Printed and distributed by:

World Health Organization
Regional Office for the Western Pacific
Manila, Philippines

October 2018
NOTE

The views expressed in this report are those of the participants of the Third Strategic and Technical Advisory Committee (STAC) for Viral Hepatitis and do not necessarily reflect the policies of the conveners.

This report has been prepared by the World Health Organization Regional Office for the Western Pacific for Member States in the Region and for those who participated in the Third Technical Advisory Committee (STAC) for Viral Hepatitis in Manila, Philippines from 17 to 20 September 2018.
CONTENTS

1. INTRODUCTION .................................................................................................................................................. 1

1.1 Meeting organization ......................................................................................................................................... 1

1.2 Meeting objectives ............................................................................................................................................. 1

2. PROCEEDINGS ...................................................................................................................................................... 1

2.1 Opening session ................................................................................................................................................ 1

2.2 Joint STAC-ERP plenary session Day 1 ........................................................................................................ 2

2.3 STAC session-1: Accelerating prevention, testing and treatment ................................................................. 5

2.3.1 Mid-term progress – gaps and opportunities ............................................................................................ 5

2.3.2 Promoting testing: Finding the missing millions ...................................................................................... 6

2.3.3 Access to hepatitis medicines: update ........................................................................................................ 6

2.3.4 Elimination of hepatitis in Japan: prevention and treatment beyond the general population to reach the unreached ......................................................................................................................... 7

2.4 Session 3: Health systems and viral hepatitis ................................................................................................. 8

2.4.1 Financing hepatitis services ....................................................................................................................... 8

2.4.2 Laboratory services for hepatitis - report from the Informal Consultation on the Quality Improvement of Laboratory Service for Viral Hepatitis ......................................................................................... 8

2.4.3 Global reporting and strategic information for viral hepatitis ..................................................................... 9

2.4.4 Estimating burden of disease and cascade of care – modelling and programmatic data ........................................... 9

2.5 Session 4: STAC – review of the TOR, election of new chairs and STAC’s way of working ...................... 10

2.6 Joint STAC-ERP plenary session Day 2 ........................................................................................................ 11

2.6.1 Maternal, newborn and child health (MNCH) and viral hepatitis: fostering collaboration between MNCH, EPI and HSI ........................................................................................................................................... 11

2.6.2 HBV EMTCT modelling in China ................................................................................................................ 11

2.6.3 Cost effectiveness analysis of triple EMTCT in Cambodia ......................................................................... 11

2.6.4 Communication activities for hepatitis ........................................................................................................ 12

2.6.5 Preventing healthcare-associated infections and vaccination for healthcare workers in China ............ 12
2.6.6 Preventing healthcare-associated infections and vaccination for healthcare workers ...........................12

3. HBV elimination of mother to child transmission ..................................................................................13

3.1 Session 1: Understanding the evidence for EMTCT of HBV: Interventions for EMTCT – antenatal screening and use of HBIG, antivirals and post-vaccination serologic testing (PVST) .........................................................14

3.1.1. Current evidence and research findings on EMTCT HBV interventions..............................................14

3.3.2 Preliminary findings from ongoing studies .........................................................................................14

3.3.2.1 SHIELD zero transmission HBV EMTCT project, China ....................................................................14

3.3.2.2 Pragmatic HBIG-free regimen: ANRS TA PROHM Cambodia ...........................................................15

3.3.2.3 Victoria Perinatal HBV prevention project, Australia ........................................................................15

3.3.3 Existing guidance for EMTCT interventions of HBV in countries ....................................................16

3.2 Assessment and validation of EMTCT .................................................................................................17

3.2.1 Lessons learned from validation of HIV and syphilis ........................................................................17

3.2.2 Proposed impact and programming metrics in Framework for Triple Elimination and validation of HBV EMTCT .................................................................17

4. Recommendations ................................................................................................................................18

5. Recommendations from the HBV EMTCT .............................................................................................19

ANNEX 1: Provisional List of Participants, Temporary Advisers, Representatives/Observers and Secretariat ..25

ANNEX 2: Meeting Agenda .........................................................................................................................29

Keywords:

Hepatitis, Viral, Human – prevention and control / Hepatitis B / Hepatitis C / Hepatitis B vaccines / Regional health planning / Immunization / Vaccination
SUMMARY

There has been tremendous progress in the prevention of hepatitis, in particular hepatitis B through immunization with the Western Pacific Region achieving its target of HBV control ahead of time. However, the Western Pacific Region bears almost half the global burden of people living with chronic hepatitis B and C, and most people do not know they are infected. Treatment access remains low despite dramatic reductions in the cost of antiviral drugs and improved availability of lower cost generic HCV direct-acting antivirals (DAAs) and HBV treatment. The Third Strategic and Technical Advisory Committee (STAC) for Viral Hepatitis was held at the Western Pacific Regional Office of the World Health Organization, Manila, Philippines from 17 to 20 September 2018. The consultation was held jointly with the Sixth Hepatitis B Immunization Expert Resource Panel (ERP). Joint sessions were held between the two groups to discuss a wide range of issues related to the implementation of the Regional Action Plan for Viral Hepatitis in the Western Pacific 2016-2020. Concurrently, the meeting included focussed discussions on HBV elimination of mother-to-child transmission (EMTCT) including the criteria for validation of elimination and opportunities for synergies and joint work between ERP and STAC. Recommendations included opportunities for improving synergies through integrated service delivery to scale-up testing and treatment including triple EMTCT interventions under the umbrella of universal health coverage (UHC), improving hepatitis reporting within current data systems, strengthening laboratory capacity and quality assurance systems, and providing platforms for information sharing and partnerships.
1. INTRODUCTION

1.1 Meeting organization

The Third STAC for Viral Hepatitis was held at the Western Pacific Regional Office of the World Health Organization, Manila, Philippines from 17 to 20 September 2018. The consultation was held jointly with the Sixth Hepatitis B Immunization ERP. The meeting was organised for the STAC to review midterm progress on implementation of the Regional Action Plan for Viral Hepatitis in the Western Pacific 2016-2020 and discuss recommendations and next steps including cross-cutting issues between the STAC and ERP. The STAC and ERP further discussed joint objectives including additional interventions to eliminate mother-to-child transmission (MTCT) of hepatitis B, building upon high vaccine coverage, developing recommendations for global criteria and process for validating EMTCT of hepatitis B and discussing the ERP and STAC’s involvement in this process. The list of the participants is available in Annex 1, and the meeting agenda is outlined in Annex 2.

1.2 Meeting objectives

The STAC meeting objectives were to review the midterm progress on implementation of the Regional Action Plan for Viral Hepatitis in the Western Pacific 2016-2020 and to discuss recommendations and next steps including cross-cutting issues between the STAC and ERP; and the joint objectives for the STAC and ERP were:

- to discuss additional interventions to eliminate MTCT of hepatitis B, building upon high vaccine coverage; and
- to develop recommendations for global criteria and process for validating EMTCT of hepatitis B and discuss the ERP and STAC’s involvement in this process.

2. PROCEEDINGS

2.1 Opening session

Dr Naoko Ishikawa welcomed the participants as the Responsible Officer for the Third Strategic and Technical Advisory Committee for Viral Hepatitis and Sixth Hepatitis B Immunization Expert Resource Panel Joint Consultation.

Dr Mark Jacobs, acting Deputy Programme Manager, delivered opening remarks on behalf of Dr Shin Young-soo, WHO Regional Director for the Western Pacific. Dr Jacobs welcomed participants to the joint consultation of the third STAC for viral hepatitis and sixth ERP. He acknowledged the progress in the Western Pacific Region (WPR) and government commitment to addressing hepatitis. World Hepatitis Day was celebrated in Mongolia this year, marking the success in combating viral hepatitis through providing universal coverage for diagnosis and treatment for the entire population through the national health insurance programme. However, there are many more people who need to be tested and linked to care and treatment, given the substantial burden in the WPR. Dr Jacobs encouraged participants to review progress and lessons learned and recommend ways in which the WPR can meet the targets of
the Regional Action Plan for Viral Hepatitis in the Western Pacific 2016-2020 to reduce morbidity and mortality due to hepatitis. After the introductory address, Dr Rosmawati Mohamed from Malaysia and Dr Henry Chan from Hong Kong, China were nominated and accepted as co-chairs for the STAC meeting. Dr Janus Ong (Philippines) stepped in to replace Dr Chan on Day 1.

2.2 Joint STAC-ERP plenary session Day 1

Dr Marc Bulterys presented an overview of hepatitis B prevention and global progress towards elimination of viral hepatitis. To eliminate viral hepatitis as a public health threat by 2030, which includes reductions in incidence by 90% and mortality by 65%, will require addressing gaps in prevention particularly coverage of the timely hepatitis B vaccine birth dose (HepB-BD, defined as HepB-BD given within 24 hours of delivery), harm reduction for people who inject drugs (PWID), HBsAg testing and ensuring access to affordable treatment at scale. Administration of the timely HepB-BD has resulted in major success in the WPR where perinatal transmission historically was a major problem. However, global coverage was still low at 39% by 2015 and even lower in the African region which is highly endemic for hepatitis B virus (HBV). Vaccine coverage for the third dose of HBV vaccine (HepB3) improved globally to about 84% in 2017. Dr Bulterys noted the substantial burden of chronic HBV and HCV infection particularly in low and middle income countries, and the disproportionate burden of HBV in the WPR. Low cost generic medicines for HBV treatment are now widely available, however countries still need to work on making treatment accessible. Global cascades of HBV and HCV care show that many infected individuals remain undiagnosed and only a minority are accessing treatment. WHO's focus includes delivering for country impact; addressing data, normative and policy needs; and positioning the hepatitis response within the broader UHC agenda.

Dr Joseph Woodring outlined the progress of HBV control through immunization in the WPR, which has prioritized actions to combat HBV for more than two decades. He noted that twenty-four countries in the Western Pacific Region have evidence from the serosurveys of meeting the target of <1% HBsAg seroprevalence among 5-year-old children. This target was set for achievement regionally by 2017 and globally by 2020. The WPR as a whole has met this <1% target, with 0.93% HBsAg prevalence among children born in 2012. HepB3 coverage has increased globally, with the WHO Western Pacific Region demonstrating the highest HepB3 coverage. Coverage of the HepB-BD, while improving in the Western Pacific Region and the Region of the Americas, remains low in most other regions.

For countries which have met the target of ≤1% HBsAg seroprevalence among 5-year-old children, new methodologies for verification will be required as traditional serosurveys will no longer be feasible. Possible methods include using programme data to estimate the MTCT rate to help evaluate progress towards EMTCT of HBV. Coverage of institutional delivery in the WPR is 89%, and studies show that newborns are more likely to receive the timely HepB-BD if they are born in health facilities compared to home deliveries. The Regional Committee’s 2017 endorsement of the Regional framework for the triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis in Asia and the Pacific, 2018-2030 looks to use the shared Reproductive, Maternal, Newborn, Child and Adolescent Health (RMNCH) platform to coordinate and efficiently enable elimination of mother-to-child transmission (EMTCT) of these three infections.

Dr Woodring discussed the use of heat-stable HepB-BD outside of the cold chain (OCC) in areas which are hard to reach and or have limited cold chain capacity. He surmised that reaching the 2030 global
target of <0.1% HBsAg prevalence among 5-year-old children will require hepatitis B control interventions beyond high immunization coverage, such as antiviral treatment for pregnant women with high hepatitis B viral load and hepatitis B immunoglobulin (HBIG) and post-vaccination serological testing (PVST) for HBV-exposed infants. These additional hepatitis B interventions require coordination across other programmes such as RMNCH and HIV, Hepatitis and Sexually Transmitted Infections (HSI).

Dr Po-Lin Chan presented the progress of implementation of the Regional Action Plan for Viral Hepatitis in the Western Pacific 2016-2020. The WPR shoulders 40% of the global burden of people living with HBV and HCV, and one-third of global viral hepatitis-related deaths. She noted the success and high coverage of prevention interventions to date, noting that 85% regional coverage of timely HepB-BD far exceeds that of any other region, though many countries remain below the 95% target for 2017. Harm reduction among people who inject drugs has also fallen short of the 2017 milestone.

Opportunities exist to leverage the synergies of integrated service delivery such as through triple EMTCT. Countries are now working on strengthening their comprehensive response on hepatitis prevention and treatment, and 21 countries have developed or are developing national action plans. HBV and HCV treatment are being financed through health insurance and government financing in 11 countries. In 2016, modelling of the cascades of care for the region indicated that overall testing coverage for HBV and HCV were 17% and 21%, respectively; however treatment access was low. The challenge in scaling-up testing, linkage to care and ensuring affordable treatment access remains. There are opportunities to reduce drug costs through use of lower cost generic medicines. Barriers to access for hepatitis care such as stigma and discrimination remain poorly understood in most countries.

Dr Naoko Ishikawa provided an overview of the Regional framework for the triple elimination of mother to-child transmission of HIV, hepatitis B and syphilis in Asia and the Pacific, 2018-2030, endorsed by Member States in October 2017. With benefits to the individual and their family, the framework calls for high level commitment on quality maternal, newborn and child health (MNCH) services; building more efficient and sustainable mechanisms for integrated service delivery, as well as prevention of other perinatally transmitted infections such as hepatitis C. The triple EMTCT framework draws upon the experience of dual elimination of HIV and syphilis, and includes HBV EMTCT impact indicators which are aligned with the 2030 global target of ≤0.1% HBsAg seroprevalence among 5-year-old children.

HBV EMTCT builds on the foundation of a strong HBV vaccination programme, with an incremental approach to offering additional hepatitis B interventions and services. These include universal antenatal screening of HBV, use of antiviral drugs by infected pregnant women, HBIG for their exposed babies, PVST to determine the outcome of babies, as well as opportunities for identifying and linking pregnant women and their family members with chronic HBV infection to appropriate services.

In 2017, activities included pilot projects in China, cost-effectiveness analysis in Cambodia, and developing joint action plans in other countries. Consultations conducted in China and Malaysia noted that there is a need for new combined approaches for validation of EMTCT, and that accumulating implementation experience in countries will provide evidence towards developing WHO guidance on the additional interventions and validation approaches needed. Triple EMTCT is a strong mechanism to facilitate the move towards hepatitis elimination.
Dr Hui Zheng presented China's progress on HBV prevention and EMTCT towards 'finishing the last mile'. China has adopted an increasingly rigorous approach to HBV policy since 1985, with introduction of universal antenatal HBV screening among pregnant women and HBIG to HBV-exposed babies in 2011. China also updated the HBV vaccination schedule in 2016 and began piloting the feasibility of PVST for HBV-exposed children in 2017. The focus is on ensuring universal coverage of the timely HepB-BD in hospitals and using community-based approaches for home deliveries, provision of free HBsAg testing among pregnant women and free HBIG for HBV-exposed babies. Catch-up vaccination among 68 million children and adolescents less than 15 years of age in 2009-2011 added to the success of prevention efforts. National programme data indicate 99% HBsAg testing among pregnant women, 96% coverage of timely HepB-BD, 99.5% HepB3 coverage and 99.5% HBIG coverage of HBV-exposed babies.

Dr Zheng presented lessons learned from the PVST feasibility pilot study, noting that 2.6% of HBV exposed infants remain susceptible after vaccination and need revaccination. Operational challenges in ensuring adherence to blood testing for PVST among infants were also discussed: 44% of caregivers (parents or grandparents) refused blood sampling or there was failure to obtain blood from the infant. Implementation of the PVST service needs to be supported by a strong multi-sectoral integrated information platform, ensuring that the mother's HBV status is also included within the children's vaccination information system.

China has established triple EMTCT as a national commitment and priority under the 13th five year plan for EMTCT (2016-2020) with establishment of demonstration pilot studies, development of validation guidelines, subnational preparation, resourcing and readiness for validation of EMTCT at national level. The SHIELD zero transmission of HBV EMTCT project involves selective use of maternal antivirals to further reduce MTCT of hepatitis B and networks 100 hospitals in providing this service. Next steps include strengthening timely HepB-BD implementation in low-performing areas, improving the prevention of MTCT strategy by ensuring testing of HBsAg-positive pregnant women for HBeAg and/or maternal HBV viral load, promoting selective use of antiviral drugs; strengthening monitoring and evaluation, as well as multisectoral collaboration among the national immunization programme, maternal child health services, hospital services and policy think-tanks on immunization.

Dr Anita Suleiman presented Malaysia's progress on HBV and HCV elimination. Malaysia started its hepatitis B programme in 1974 with blood donor screening, progressively expanding the programme to include surveillance in 1988, healthcare worker vaccination in 1989, screening of high-risk pregnant women receiving antenatal care (ANC) in 2000, and public advocacy work for awareness in 2008. Malaysia achieved 0.3% HBsAg national seroprevalence among children in 2011, and began acute and chronic hepatitis surveillance in 2012. In 2013, routine antenatal HBsAg screening was introduced in Sabah as HBV prevalence was high, particularly among ethnic groups and migrant populations. High risk groups for vaccination and screening include healthcare workers, police, prison inmates, and clients of drug rehabilitation centres. Programmatic data from 2009 showed HepB-BD coverage was 96%, but dropped to 87.2% in 2013 before gradually climbing to 90.2% in 2017. Malaysia was validated as having achieved the WHO HBV control target of <1% HBsAg seroprevalence among children in 2009.

There is no requirement to report HBsAg screening among women attending ANC, but a few states conducting surveys showed that HBsAg prevalence was 2.6% in 2018. Sabah province, which has the highest HBV burden in the country, achieved 64% coverage of ANC screening. HBV case notification
has been gradually increasing. Dr Suleiman surmised that to achieve HBV elimination, policy changes are needed to align with the *Regional framework for the triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis in Asia and the Pacific, 2018-2030*, including the development of guidelines for HBV EMTCT and training of healthcare providers, as well as creating demand and increasing public awareness. There are plans to pilot HBV EMTCT in three states to generate evidence for policy-making.

Regarding HCV elimination, Malaysia has worked on increasing surveillance, awareness and advocacy, prevention, and treatment access. Notified cases have increased over time, with substantial advocacy by community-based organizations, particularly PWID and men who have sex with men (MSM). In 2017, Malaysia introduced compulsory licensing for sofosbuvir and treatment for HCV using direct-acting antivirals (DAAs) was launched in 2018. Dr Suleiman noted that to achieve HCV elimination, HCV testing using point-of-care tests is required, with decentralization of treatment access, strengthening of advocacy, formation of government and NGO partnerships, training of healthcare providers and establishment of the treatment registry. The FIND projects will pilot the approach to decentralizing testing of HCV. Malaysia aims to screen 35,000 people and treat 4,500 infected individuals for HCV by 2022.

In subsequent discussions during the meeting, it was pointed out that other hepatitis infections such as hepatitis E (HEV) did not feature strongly in the agenda and it would be important to include them in the future since two candidate vaccines are in development. Participants discussed triple EMTCT and the accumulating evidence on the effectiveness of antivirals for EMTCT, noting the need for WHO guidance development in this area and inclusion in SAGE discussions. The triple EMTCT approach should be part of the broader hepatitis elimination approach articulated by the *Regional Action Plan for Viral Hepatitis in the Western Pacific 2016-2020*, and positioned within UHC and health systems strengthening.

### 2.3 STAC session-1: Accelerating prevention, testing and treatment

The STAC convened to review recommendations of the second STAC meeting in Hanoi (2016), presented by Dr Naoko Ishikawa. Participants noted progress in implementation of the recommendations and noted the positioning of hepatitis responses under UHC. The WPR will focus on achieving 2020 targets, including supporting expansion of testing services, decentralization of care and treatment, establishment of surveillance and programme monitoring and implementation of the *Regional framework for the triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis in Asia and the Pacific, 2018-2030*.

#### 2.3.1 Mid-term progress – gaps and opportunities

Dr Po-Lin Chan presented an overview of the progress, challenges and opportunities on implementing the *Regional Action Plan for Viral Hepatitis in the Western Pacific 2016-2020*. The impact of chronic hepatitis B and C in the WPR is made evident as cirrhosis and liver cancer are among the top ten leading causes of death among people over 30 years of age. Dr Chan presented the estimated burden of disease and prevalence of HBV and HCV, noting that while there are high absolute numbers of infections in populous countries such as China, Viet Nam, Philippines and Mongolia, the prevalence of HBV is particularly high in Pacific Island States. The HCV epidemic is diverse across the WPR. In order to advance the hepatitis response under UHC, the health systems perspective of the four categories of countries in the WPR is used: advanced economies, transitional economies, low and middle income and Pacific Island countries. Dr Chan provided an overview of the challenges of integrating hepatitis within
UHC including concerns over financing the substantial burden of disease, epidemic diversity and need for prioritization and equity; the inadequate response and lack of services for key populations and other at-risk groups; lack of human resources; capacity-building needs, lack of civil society involvement and limited access to services. Nevertheless, UHC provides an important opportunity as the core of UHC is service delivery, and there are pragmatic approaches to integrating and scaling-up hepatitis testing and treatment within existing programmes and services. WHO's support to countries will focus on expanding 'know your epidemic', continued advocacy for political, government and financing commitment as well as civil society engagement, technical support for programme elements such as consolidating the success of prevention interventions including integrated service delivery through triple EMTCT, and resource mobilisation and partnerships.

2.3.2 Promoting testing: Finding the missing millions

Mr Michael Ninburg gave an overview of the World Hepatitis Alliance's (WHA) campaign on promoting hepatitis testing "Find the Missing Millions". He noted that diagnosis remains one of the biggest barriers to elimination and very few countries are on track to meet the WHO's 2020 interim target of 30% of people living with hepatitis B and C diagnosed. In fact globally, only 38 countries are on track to meet the 2020 hepatitis C target and just 21 are on track to meet the hepatitis B target. Find the Missing Millions is a three-year global awareness-raising and advocacy campaign aimed at tackling the main barriers to diagnosis and scaling-up the response by putting civil society organizations and affected communities at the heart of the solution. The global survey on barriers for hepatitis testing showed that key issues included lack of public knowledge, poor awareness among healthcare professionals, lack of easily available and accessible testing, stigma and discrimination and out-of-pocket costs. Stigma remained a critical barrier with 93% of countries surveyed reporting stigma and discrimination to some degree, 72% of respondents suffered from self-stigmatization, 53% had been socially isolated, 50% had experienced unjust barriers to healthcare and 42% had lost out on job opportunities or income. The project will focus on raising awareness, making testing more accessible and removing cost barriers for viral hepatitis testing. WHA will work with members in five or six different countries to design and implement advocacy plans focusing on finding the undiagnosed and addressing barriers, contextual to the country.

2.3.3 Access to hepatitis medicines: update

Mr Giten Khwairakpam presented an update on access to hepatitis C medicines in Asia. Regulatory approvals of direct-acting antivirals (DAAs) have improved and generic pan-genotypic DAAs such as sofosbuvir and velpatasvir are now available. Indian generic manufacturers remain the major supplier globally, and there have been dramatic price reductions. However, variations in pricing of DAAs remain in Asia. As an example, generic sofosbuvir/ledipasvir costs USD 600 per bottle in Viet Nam, compared to USD 30, USD 200, USD 171 and USD 47 in Ukraine, Cambodia, Nepal and India respectively. However, generic manufacturing in Viet Nam is likely to start soon and this will reduce costs. Tenofovir disoproxil fumarate (TDF) is registered in most countries for treatment of HIV, but not for HBV treatment. Costs per bottle could be as low as USD 3.25 per month. Patent protection for TDF will end in mid-2018 in most countries and thus generic options will become available. Entecavir and Tenofovir alafenamide for HBV treatment are being registered in some countries. Mr Khwairakpam surmised that while drug prices have been markedly reduced, this does not necessarily translate to better access to treatment. Price reductions have been seen however there are wide differences in price between countries. Access to treatment for
HBV needs to be improved to achieve elimination targets, and generic drug prices for tenofovir in many countries are probably at their lowest point.

### 2.3.4 Elimination of hepatitis in Japan: prevention and treatment beyond the general population to reach the unreached

Dr Tatsuya Kanto gave an overview of elimination of hepatitis in Japan which has seen the gradual introduction of measures including nationwide screening of hepatitis introduced in 2002, establishment of the hepatitis care network linking primary to tertiary services, provision of highly subsidised treatment, and in 2018, subsidising the costs of treatment for liver cancer and decompensated cirrhosis related to HBV and HCV. While there has been success in diagnosing hepatitis, gaps remain in linkage to care and treatment. Hepatitis medical coordinating teams are now established in all 37 prefectures and will support patients to navigate through the medical system and to access care. About one million people are being tested annually for HBV and HCV with seroprevalence of HBV and HCV at 0.7% and 0.4%, respectively. In a recent national survey, public awareness of testing and treatment services was inadequate. Japan will focus on the use of innovative approaches to strengthen public awareness and knowledge, and use information technology to ensure the public knows the location of services through the "hepatitis testing navigation system". In summary, Dr Kanto noted that in order for Japan to eliminate viral hepatitis, there needs to be improved access to testing, follow-up of test-positive individuals, linkage to care and treatment services, awareness and education of the general public, commitment of local government and attention to addressing stigma and discrimination directed at people living with hepatitis.

In the discussion, participants noted the need to contextualise scale-up of testing according to a country's epidemic and financing capacity. Most countries in the region would need to offer universal voluntary testing, especially for HBV, following WHO guidelines for testing. However, financing constraints may limit this approach and many countries will need to decide priority groups for testing and treatment. Mongolia provides a good example of population-wide testing in a middle income setting with political commitment, engaged civil society and prioritization of hepatitis as a public health threat. Data reporting systems for hepatitis testing are not currently available in most countries since hepatitis screening is widely available in both private and public sector health facilities, resulting in lack of data on testing numbers. In some countries, access to treatment is not yet available and there were debates on whether it was ethical to test when treatment is not available. Most experts agreed on the benefits of knowing HBV status, in that harm reduction measures such as assessment of liver disease and education and counselling on reducing alcohol use could be provided until treatment becomes available. Stigma and discrimination and the need to improve regional and country-based advocacy was also discussed. In the Philippines, social media is used to disseminate information on where to get tested and treated. Lessons learned from addressing HIV-related stigma and discrimination should be applied to hepatitis. A less well known aspect of stigma and discrimination includes the experience of children and young people infected with hepatitis, which is a chronic infectious disease similar to HIV except that the consequences of chronic infection such as cirrhosis and hepatocellular carcinoma develop principally after the fourth decade of life. WPRO is working with several countries on surveys to document this aspect of stigma and discrimination. Experts touched upon the need for more work on testing and treatment of infected healthcare providers, particularly in the Pacific where HBV is endemic and most countries have issues with health workforce resilience. Finally, the need to increase resources to catalyse country implementation and WHO support was discussed.
2.4 Session 3: Health systems and viral hepatitis

2.4.1 Financing hepatitis services

Mr Ronald Tamangan presented a picture of the regional context highlighting the changing health needs of the population following successes in communicable and vaccine-preventable disease control, coupled with emerging pandemics, natural disasters and aging populations. There has been increasing economic growth and expectations for quality health services, low government health spending and high out-of-pocket payments; and primary care services which are often not fully enabled to meet the challenges of non-communicable diseases (NCDs) or the unfinished communicable disease agenda (including hepatitis).

He noted challenges in financing hepatitis interventions in most countries, leading to high out-of-pocket expenses. While prices of hepatitis drugs have reduced significantly, they are still relatively expensive. Many countries suffer from cash flow difficulties which results in problems in procuring hepatitis drugs, and most countries prioritize staff salaries before spending on commodities and programme costs. Taking Mongolia as an example to discuss financing of their national hepatitis programme, he noted that while health insurance shouldered the major costs of clinical care for hepatitis, challenges remain related to those people without health insurance, funding for programmatic costs and the implementation of new WHO guidelines for HCV which bring down the age of treatment to children more than 12 years old, as well as the potential mop-up of those not covered so as to achieve elimination. In summary, financing hepatitis is a work in progress and considerations include what funding mechanisms can be leveraged for which services for prevention, testing and treatment at population and individual levels.

2.4.2 Laboratory services for hepatitis - report from the Informal Consultation on the Quality Improvement of Laboratory Service for Viral Hepatitis

Dr Donghyok Kwon provided an overview of the recommendations from the Informal Consultation on the Quality Improvement of Laboratory Service for Viral Hepatitis meeting which included the results of the gap analysis on laboratory systems in eight countries (China, Brunei Darussalam, Lao People’s Democratic Republic, Mongolia, Papua New Guinea, the Philippines, Singapore and Viet Nam). The gap analysis found fewer systems in place for hepatitis compared to HIV laboratory systems. In at least half of the laboratories surveyed, no systems existed for licensing of laboratories, registration/qualification of test kits, monitoring stock out of test kits, and quality management and accreditation systems for laboratories.

Discussion included the need for increased investment in laboratory systems for hepatitis in low and middle income countries in the Region.

Main recommendations for Member States were to consider developing national strategic plans on strengthening laboratory services for both clinical and public health (surveillance) purposes, establish and support development of in-country quality assurance systems, identify key national laboratories that can facilitate external quality assurance (EQA) in-country, use EQA as an opportunity to improve services by providing feedback and refresher courses to laboratories, learn from the experiences of HIV testing services, adapt and implement WHO testing guidelines for viral hepatitis B and C, and ensure the availability of human resources for quality management. Main recommendations for WHO included advocacy for investing in quality laboratory services through domestic financing; improve partnership and collaboration among laboratories in the region; make quality assurance systems more efficient and sustainable by reducing duplication; and strengthen dissemination of information and provide support to countries with interested diagnostics manufacturers to enhance applications for the WHO prequalification
programme. Next steps include establishing effective communications channels among WHO, country laboratories and partners and creating an informal technical working group for hepatitis testing.

2.4.3 Global reporting and strategic information for viral hepatitis

Dr Linh-Vi Le provided an overview of the ten core indicators along the results chain for hepatitis monitoring. WHO recommends systems for hepatitis surveillance (acute hepatitis that reflects new infections, chronic hepatitis and sequelae surveillance) and programme data (prevention indicators and patient registries for the cascade of care and cure) and has developed protocols which are available on the website (https://www.who.int/hepatitis/publications/en/). WHO is developing a guide for establishing data systems for the cascade of care which includes prevention indicators reported by other programmes such as HIV, EPI and MNCH. Currently most countries rely on modelled data as they either lack reporting systems, or have databases which have not yet integrated hepatitis reporting. WHO online tools to estimate the cost effectiveness of treatment to support the case for UHC of hepatitis treatment are available at www.hepbcalculator.org and www.hepccalculator.org. The global reporting system for hepatitis (GRSH) has recently been launched and provides country-specific dashboards to visualise data, as well as capturing data missing from other reporting systems including data on policy framework and national guidelines, cascade of care and the fraction of cirrhosis and hepatocellular carcinoma attributable to HBV and HCV. Dr Le noted that national surveillance systems for hepatitis in the region are at various stages of development. The global online reporting tool was recently established with the hope that countries will set up systems which will support obtaining cascade data. There is need to move away from reliance on modelling to establishing strong and sustainable surveillance and reporting for hepatitis.

2.4.4 Estimating burden of disease and cascade of care—modelling and programmatic data

Mr Homie Razavi presented, through teleconference, the modelling approach used by the Polaris Observatory to estimate hepatitis cascade of care at the national, regional and global levels for HBV and HCV. He noted the challenge of modelling which is dependent on data inputs. Several core inputs for HCV include: HCV prevalence by age, HCV genotype, and numbers diagnosed and treated, including sources of data. For HBV modelling, core inputs are: HBsAg by age, HBeAg prevalence and screening among pregnant women, historical vaccination schedules and coverage, and numbers diagnosed. Modelling can take into account the impact of time (aging, mortality, disease progression and response to treatment). There is a considerable amount of information which has never been published thus having a structured approach to engaging countries and their experts is critical. Models which are properly built and calibrated can forecast future prevalence and burden with surprising accuracy. Multiple sources of data including cancer registries should be used, with the caveat of understanding their limitations. In summary, modelling is a very cost effective way of estimating the epidemiology of HBV and HCV at a point in time, and the number of data inputs required for modelling is generally manageable in most countries.

Dr Ben Cowie talked about estimating the burden of disease and cascade of care based on Australia's experience of the use of programmatic data and modelling. As Australia does not have a unified national reporting system for hepatitis, it was necessary to map the data source, purpose of the database and possible use for surveillance and monitoring for hepatitis. Australia's national reporting is based on an analysis of programmatic and public datasets for HBV and HCV. He noted that routinely collected data can be used for policy and action, for example to identify priority populations such as those at risk;
hotspot mapping by region and geographical area; reporting on cascade of care including addressing disparities in access to treatment; identifying drivers of access such as prescription of HCV treatment by providers other than specialists; and making data work for elimination such as using an interactive online mapping tool. Australia also uses modelling to estimate burden, access to testing and treatment, and mortality attributable to chronic hepatitis. Dr Cowie noted that there is a need for new approaches for notification for disease surveillance linked to improving access to care. Currently, HBV and HCV viral load tests results are only notifiable by a laboratory if positive and only once per patient. Discussions are underway to modify regulations to make all HBV and HCV viral load results notifiable irrespective of result, as this would allow surveillance-based monitoring of treatment/cure/reinfection for HCV; and viral suppression for HBV, potentially indicating need for treatment and identifying pregnant women with high viral load. There are existing examples of the use of surveillance systems to link to care and coordinate care at public health level including the US Perinatal Hepatitis B Prevention Program, and New York City's HCV surveillance-based linkage to care and cascade analysis.

Discussions indicated consensus that understanding the epidemiology and disease burden is a pre-requisite for developing national action plans. Strategic information should be included in national action plans with the understanding that improvement is an iterative process to develop data and evidence for decision making. Programme data and modelling approaches complement each other. The focus for most countries should be on developing the care cascade and using this as a starting point to understand the current situation and decide further action. Mapping of data sources would be a good start for countries. As there is a diversity of lessons and experiences, WHO should consider documentation of country case studies for the different areas including for strategic information.

2.5 Session 4: STAC – review of the TOR, election of new chairs and STAC's way of working

Dr Po-Lin Chan provided an overview of the functions of the STAC which are to contribute to the regional viral hepatitis response by providing independent state-of-the-art scientific, strategic and technical advice. Members of the STAC are appointed by the Regional Director on the basis of their technical expertise and scientific and public health experience in viral hepatitis and may submit to the Regional Director technical documents, reports and recommendations as deemed necessary. The STAC members were introduced, including those experts who were unable to attend. Discussions included the STAC's working methods, taking into account evolving regional needs and demands and declining funding for meetings, and ways in which STAC members can support regional work. STAC members felt that the current terms of reference were still relevant. The STAC supported the proposal to have biannual face-to-face meetings, alternating with either virtual consultations or side meetings arranged during major regional hepatitis conferences. Dr Rosmawati Mohamed and Dr Henry Chan were unanimously voted to continue as co-chairs for the STAC.
2.6 Joint STAC-ERP plenary session Day 2

2.6.1 Maternal, newborn and child health (MNCH) and viral hepatitis: fostering collaboration between MNCH, EPI and HSI

Dr Fuqiang Cui presented the approach and experience of cooperation between different health departments in China. The China Centers for Disease Control and Prevention (CDC), Maternal Child Health (MCH) and general and infectious disease hospitals interact with each other and have synergistic impact for HBV EMTCT to improve the health of mother and child. The national immunization programme and MCH have agreed a strategy to improve administration of the timely HepB-BD following the principle of "who delivers the baby is responsible for birth-dose vaccination". Subsequent doses of HBV vaccine are the responsibility of the immunization programme, which has undertaken further programmatic strengthening including improving vaccine availability in all hospitals and township health facilities, supervision of the operational principle as above, education for parents and healthcare providers on the need for the timely birth dose, as well as intensifying training, supervision and monitoring of county, township and village healthcare workers. Collaboration includes the SHIELD zero transmission of HBV project which networks 107 hospitals across the country to deliver antivirals to a subset of HBV-infected pregnant women with high maternal viral load. The National Immunization Advisory Committee (NIAC) is a high level policy think-tank for immunization that advises government on vaccine-based prevention and control. A working group on HBV has been established and has the membership of clinicians, the national immunization programme and MCH, who work together on HBV EMTCT policies based on pragmatic field experience of integrated delivery through triple EMTCT. Through the national MCH plan, demonstration pilots in three provinces have been launched which will contribute to evidence building on HBV EMTCT in China.

2.6.2 HBV EMTCT modelling in China

Dr Tim Hallett presented the results of HBV EMTCT modelling in China, which has been used to look at: the current and future projected burden of HBV; achievement of the target of 0.1% HBsAg prevalence among children; strategies which can bring forward the date of EMTCT; how to measure where the country is on course for success; the case for treatment expansion; and formulating economic arguments for policy making. Modelling suggests that based on current intervention strategies and levels, there will be a projected 139 million new cases of hepatitis B infection between 2018 and 2050 and that China could achieve the global target of 0.1% HBsAg prevalence among children by 2027. Catch-up campaigns and targeted vaccination among healthcare providers and hemodialysis recipients will have no appreciable effects on population-level HBV epidemiology but may have individual-based protective effects. The model estimates that the addition of antiviral drugs for HBeAg-positive pregnant women would lead to substantial gains in reducing new infections and that the country could reach the 0.1% HBsAg prevalence among children target by 2023. Achievement of this target by 2025 would be predicted by an MTCT rate among HBsAg-positive mothers <2.25% and among HBeAg-positive mothers <6.5% in 2020. Dr Hallett noted that access to treatment must be increased concomitantly to prevent deaths among the large number of adults already infected and that this would have a strong positive return-on-investment.

2.6.3 Cost effectiveness analysis of triple EMTCT in Cambodia

Dr Lei Zhang presented an economic evaluation tool to assess the cost effectiveness of an integrated approach to triple EMTCT. Based on a decision tree analysis, the tool evaluates the potential reduction in
investment brought about by the integrated approach as a result of resource pooling and improvements in service coverage and coordination, and assesses the cost required to avert one infection in exposed infants. The tool was constructed using Microsoft Excel and ratified on simulated epidemiological data that resembles epidemics in Asia-Pacific countries. Results from the modelling conducted in Cambodia show that the integrated approach, using antenatal, perinatal and postnatal care as a platform in Cambodia for triple EMTCT of HIV, HBV and syphilis, is highly cost-effective and efficient.

2.6.4 Communication activities for hepatitis

Dr Samuel So provided an overview of communications in hepatitis. The Asian Liver Center (ALC) at Stanford University was founded in 1996 to address the disproportionately high burden of chronic HBV and liver cancer in Asians and Asian Americans and the gaps in hepatitis B and liver cancer awareness, research and national policies. The ALC has a branch in China working on year-round activities to educate the public on HBV. The Jade Ribbon Campaign, initiated by Stanford University ALC, is an international movement which helps spread awareness internationally about hepatitis and liver cancer. ALC designs campaigns and education activities to promote awareness and eliminate stigma and discrimination through social media and events, including around World Hepatitis Day. ALC has engaged with 31 multinational corporations to participate in World Hepatitis Day education in Asia and the Pacific. Community programmes bring young people from universities to educate school students across China on HBV knowledge and prevention. The programme has reached over 30,000 people. He noted that more is needed to promote public awareness and education in order to combat stigma and discrimination.

2.6.5 Preventing healthcare-associated infections and vaccination for healthcare workers in China

Dr Fuqiang Cui outlined the experience of developing a healthcare worker (HCW) vaccination programme in China. The São Paulo Declaration on Hepatitis made during the World Hepatitis Summit 2017, called upon governments to include hepatitis B vaccination for HCWs in national immunization programs. HBV vaccination is now mandatory for all HCWs in Australia, Austria, Belgium, Canada, Czech Republic, Germany, Greece, Holland, Ireland, Italy, Poland, Slovakia, Sweden and the USA, as well as for specific HCWs in direct contact with patients or body fluids in France. In China, the national action plan for viral hepatitis 2017 encourages provincial authorities to provide vaccination for healthcare workers, however, there is no national vaccination policy at present. Limited data on coverage of vaccination presents a challenge for policy-making. Dr Cui presented results from the multi-province survey among 4168 healthcare providers and noted that self-reported coverage of at least one-dose of hepatitis B vaccine was high (86%) although only 60% reported completion of the 3-dose schedule. Low vaccination coverage was noted among healthcare providers older than 40 years of age. Interestingly, one-fifth of healthcare providers refused vaccination due to concerns about vaccine safety and efficacy. In order to develop national policy, decisions about which HCWs should receive vaccination and promotion of awareness and education of healthcare providers would be required.

2.6.6 Preventing healthcare-associated infections and vaccination for healthcare workers

Dr Ben Cowie presented an overview of WHO guidance on preventing healthcare-associated infections and vaccination for HCWs. The Global Health Sector Strategy on Viral Hepatitis 2016-2021 states priority actions for countries and actions for WHO to strengthen implementation of occupational health measures that address the risk of viral hepatitis transmission in healthcare settings and the needs of health
workers living with viral hepatitis. The *Regional Action Plan for Viral Hepatitis in the Western Pacific 2016-2020* has regional milestones on national policies for vaccination of HCWs and healthcare students. Current WHO guidelines for HBV include recommendations for infected HCWs with special considerations for screening, vaccination and treatment. Dr Cowie outlined essential interventions, including universal precautions/injection safety/infection control, vaccination of susceptible healthcare providers and students as well as the need for booster doses of hepatitis B vaccine. Aspects which require discussion include pre-vaccination and post-vaccination testing, approaches to previous vaccination, and management of HBV-infected HCWs including confidentiality, prevention of discrimination and protection of workers’ rights. He noted that consideration should be given to developing a healthcare provider testing/vaccination/management implementation guide for countries to discuss options, advantages and disadvantages, emphasizing an incremental approach which can be considered depending on resources and capacity. It should be recognised that HBV is not an isolated issue of concern to healthcare providers, who are susceptible to other blood-borne infections; recommendations should include HCV testing and cure, HIV testing and antiretroviral treatment and protecting the health workforce, as part of strengthening health systems resilience and delivery of safe care to patients.

The Chairs of the ERP and STAC reported back on recommendations of the group. Joint recommendations are summarized in the section below. Refer to recommendations from ERP in the ERP meeting report.

### 3. HBV elimination of mother to child transmission

Dr Naoko Ishikawa opened the joint consultation to discuss HBV EMTCT interventions, criteria and process of validation. Regional guidance exists for verification of achievement of the regional target (<1% HBsAg prevalence among children) while there is ongoing discussion on additional interventions for EMTCT of HBV at global level. Global guidance for validation has yet to be developed. More countries are requesting for WHO guidance for operationalisation of the *Regional framework for the triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis in Asia and the Pacific, 2018-2030* and criteria for validation of EMTCT. Consultations in China and Malaysia noted the need to: develop methods for measurement towards validation of HBV control below 1%; consider the use of MTCT rates for validation to document the success of EMTCT consistent with 0.1% prevalence of HBsAg among children; develop process indicators for different interventions used in countries considering the local context; develop integrated global guidance and tools for validation of triple EMTCT; and establish strategic information and modelling reference groups for hepatitis to facilitate the application of models at the country level. The objective of the two day meeting was to discuss additional interventions to eliminate MTCT of hepatitis B, building upon high vaccination coverage, develop recommendations for the global criteria and process for validating EMTCT of HBV, and discuss the ERP and STAC’s involvement in this process. The expected outputs are recommendations for interventions, monitoring and assessment of EMTCT of HBV to be incorporated in the regional operational document.
3.1 Session 1: Understanding the evidence for EMTCT of HBV: Interventions for EMTCT – antenatal screening and use of HBIG, antivirals and post-vaccination serologic testing (PVST)

3.1.1. Current evidence and research findings on EMTCT HBV interventions

Dr Marc Bulterys presented current evidence and research findings on HBV EMTCT. Current WHO 2015 hepatitis B treatment guidelines do not have formal recommendations on the use of antiviral medicines for prevention of MTCT; the principle indication for using antivirals should be necessity for the mother’s health. At the time of preparing the guidelines, systematic reviews showed low quality evidence; limited comparisons of antivirals, evaluation of potential harms and real world feasibility studies; and unclear programmatic implications. However, more evidence is now available on the use of antiviral therapy for HBV prevention of MTCT (PMTCT) generated through systematic reviews and ongoing HBV EMTCT trials of antivirals without HBIG. The American Association for the Study of Liver Diseases (AASLD) recommends the use of antivirals particularly among pregnant women with high maternal hepatitis B viral load, to reduce the risk of perinatal transmission. HBIG in addition to the 3-dose vaccination schedule prevents more MTCT transmission than vaccine alone if the mother is HBeAg-positive, however administration of HBIG does not prevent all infant infections – studies report 2% to 12% transmission. Two clinical trials are in progress evaluating the use of maternal antiviral prophylaxis to decrease fetus/infant exposure to maternal HBV in utero and during the intrapartum and postpartum periods; and to provide the fetus and newborn with pre-exposure prophylaxis since antivirals pass the placenta barrier and vaccine/HBIG escape mutants are sensitive to antivirals. Tenofovir disoproxil fumarate (TDF) is the preferred drug. There are opportunities for synergies within triple EMTCT where the validation criteria and mechanisms consider both mothers and their babies. Methods to measure HBsAg prevalence among children when levels fall to around 0.1% are still under development but could include modelling of impact on the basis of service coverage validated by empirical data in selected countries, and surveys among children aged 4-6 years together with prospective cohorts of exposed babies followed until 12 or 18 months of age. These options are still in discussion. The next steps that WHO will work on are to consolidate effectiveness data, assess potential harms of antiviral drug use in pregnancy, review programmatic experience and feasibility as well as maternal preferences and acceptability.

3.3.2 Preliminary findings from ongoing studies

3.3.2.1 SHIELD zero transmission HBV EMTCT project, China

Dr Jinlin Hou presented the SHIELD zero transmission of HBV project which has the vision of a generation free of HBV. China has about 1 million HBV-infected pregnant women and an overall prevalence of HBsAg of 6.2% among pregnant women in 2016. The SHIELD project was designed to have a structured approach: establishing the baseline situation (through a prospective observational study in ten hospitals), linking a collaborative network of 100 hospitals to deliver HBV EMTCT including the use of antiviral drugs supported by a mobile app, with phase-3 aiming to implement an enhanced standard of care for EMTCT through establishing models for community delivery of HBV EMTCT linked to the national triple EMTCT initiative. Dr Hou presented findings of the multicentre prospective observational study in 10 hospitals, which showed high follow-up rates (92%) of hepatitis B-exposed infants at 12 months after delivery: 63% of mothers were HBeAg-positive, and 55% had HBV viral load more than 10 log 6 IU/ml. Coverage of the timely HepB-BD was 99% and HBIG was 99.8%. Analyses showed missed opportunities in care: 27% of pregnant women with high hepatitis B viral load did not receive antivirals
while 20% of those women with viral load below the threshold received antivirals. Most (75%) women received telbivudine, while only 21% received TDF because TDF was still an out-of-pocket expense. Very few children (eight children) were infected – 1.6% of infants born to mothers with high maternal viral load. Dr Hou presented the collaborative network of 10 centres of excellence with 118 networked hospitals, and use of a mobile app to connect the network of physicians: currently the app serves 20,298 pregnant women and 1448 doctors. The SHIELD project is established as a provincial demonstration pilot study as part of triple EMTCT in three counties which have hospital to community integrated management systems.

### 3.3.2.2 Pragmatic HBIG-free regimen: ANRS TA PROHM Cambodia

Dr Olivier Segeral presented the ANRS 12345 TA PROHM Cambodia study which is one of the HBIG-free clinical trials. The objective is to assess the effectiveness of a strategy using rapid tests for HBsAg and HBeAg to screen for hepatitis B infection among pregnant women, TDF-based treatment for women with a positive HBeAg test given from 24 weeks of gestation (including a test-and-treat strategy for those seen later in pregnancy), and early hepatitis B vaccination for all infants at birth (<2 hours). The outcome is the proportion of active HBV infection in infants at 6 months of age. The study will recruit over 1000 HBV-infected pregnant women. Among infected women, liver disease is assessed 6 weeks postpartum, and includes serology, APRI and FIB4 scores as well as liver ultrasound and transient elastography. The decision to stop or continue antiviral treatment will be made by an external committee. Dr Segeral noted that currently implementation shows good acceptability for the screening test. However, because blood samples need to be centrifuged, there would be issues with operational scale-up. Recently, rapid diagnostic tests licensed for whole blood use (finger prick) have become available, and there are plans to conduct validation studies. Challenges include difficulty in implementing synergies between the different health services, and implementing trial protocols in maternity wards with different working conditions. There was some shortage of HBV monovalent vaccine and the study provided vaccines to fulfil the shortage.

### 3.3.2.3 Victoria Perinatal HBV prevention project, Australia

Dr Nicole Romero presented the use of data linkage to measure PMTCT of hepatitis B in Victoria, Australia. Currently there is no national monitoring or reporting aside from HepB3 vaccination. A study in Victoria showed that only 15% of HBV-infected pregnant women had their HBeAg status assessed and 28% had their viral load quantified. Among HBV-exposed babies, only 80% received HBIG within 12 hours of birth, and 89% received the timely HepB-BD within 24 hours of birth. The project aims to assess progress towards the EMTCT of hepatitis B in Victoria through the collection, linkage, analysis and interpretation of available data. Specific objectives were to establish accurate estimates for the prevention of MTCT for hepatitis B through timely and accurate data collection, linkage and analysis, investigate hospital-level system factors associated with delivery of appropriate pre-and post-pregnancy care to women living with hepatitis B, and explore current clinical and community understandings, attitudes, and practices in relation to prevention of MTCT of hepatitis B in Victoria. The data linkage project was conceived because existing data collection systems are robust but data collection occurs in silos, and there is no political or financial will to create a new register or adapt an existing one. The cascade of care for pregnant women and HBV-exposed infants is unknown. Data sources were mapped for available indicators, and linked by name, date of birth and address. The final data for researchers is de-identified. Data linkage is possible in Australia because health data legislation (Health Records Act 2001) provides
the framework to protect the privacy of individuals' health information, and regulates collection and handling of health information. Data systems are robust and representative, with identifiable information and coverage of the majority of the population, although data entry errors or duplication may still occur. The main challenges are the lack of a unique identifier, incomplete names or dates of birth, name changes, unwillingness among data custodians to share data, and the length of time needed for linkage. Next steps are to use data for action and feedback results to stakeholders and hospitals, advocacy for funding, registry for case management and follow-up and ensuring sustainability for ongoing monitoring and evaluation of MTCT.

### 3.3.3 Existing guidance for EMTCT interventions of HBV in countries

Dr Naoko Ishikawa presented the current existing guidelines for HBV EMTCT in selected countries and guidelines showed below:

<table>
<thead>
<tr>
<th></th>
<th>testing</th>
<th>antivirals</th>
<th>eligibility</th>
<th>timing</th>
<th>drug</th>
<th>HBIG for exposed infants</th>
<th>Post-vaccination serologic testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO*</td>
<td>X</td>
<td>to be developed</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Australia</td>
<td>X</td>
<td>X</td>
<td>X (HBV DNA &gt;10^7 IU/mL)</td>
<td>28–32 weeks of gestation through 4 weeks postpartum</td>
<td>TDF</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>China</td>
<td>X</td>
<td>X</td>
<td>X (urban)</td>
<td>HBV DNA &gt; 2x10^6 IU/mL</td>
<td>24–28 weeks gestation till birth</td>
<td>TDF</td>
<td>X</td>
</tr>
<tr>
<td>Japan</td>
<td>X</td>
<td>X</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Korea</td>
<td>X</td>
<td>X</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Malaysia</td>
<td>X</td>
<td>X</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Mongolia</td>
<td>X</td>
<td>X</td>
<td>X (HBV DNA &gt;10^6 IU/mL)</td>
<td>28-32 weeks of gestation through 4 weeks postpartum</td>
<td>TDF, 3TC, or TBV</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Thailand</td>
<td>X</td>
<td>X</td>
<td>HBsAg (+) or HBV DNA &gt;200,000 IU/mL</td>
<td>28-32 weeks of gestation through 4 weeks postpartum</td>
<td>TDF</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>United States (or AASLD)</td>
<td>X</td>
<td>X</td>
<td>HBV DNA &gt;200,000 IU/mL</td>
<td>28–32 weeks of gestation</td>
<td>TDF, 3TC or TBV</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>APASL</td>
<td>X</td>
<td>X</td>
<td>HBV DNA &gt;10^{-5} IU/mL</td>
<td>28–32 weeks of gestation till birth</td>
<td>TDF or TBV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EASL</td>
<td>X</td>
<td>X</td>
<td>HBV DNA levels &gt;200,000 IU/mL or HBsAg levels 4 log_{10} IU/ml</td>
<td>24–28 weeks of gestation through up to 12 weeks postpartum</td>
<td>TDF</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3.2 Assessment and validation of EMTCT

3.2.1 Lessons learned from validation of HIV and syphilis

Dr Nathan Shaffer presented current validation mechanisms including the background and criteria for EMTCT validation, structure and processes and the new path to elimination (PTE) for high burden countries, as well as lessons learned from country validations. He noted that it was important to define key interventions and case definitions including how data was derived. EMTCT validation was based on PAHO's initiative to establish EMTCT goals for 2015. The Orange Book for validation of EMTCT (Global guidance on criteria and processes for validation: Elimination of mother-to-child transmission of HIV and syphilis), articulating core impact and process indicators, was developed initially in 2014 and revised in 2017. Dr Shaffer discussed what validation criteria mean and what is felt to be a low enough threshold to affirm that new infections in children are eliminated as a public health problem, whilst being consistent with other public health programmes. In 2017, guidance for PTE was developed for high-burden countries (maternal HIV prevalence >2% and maternal syphilis prevalence >1%). It proposes a stepwise approach recognizing gold, silver and bronze tiers of progress (for both HIV and syphilis) as intermediate benchmarks towards validation of EMTCT. Standardized tools and national report templates help countries to report towards validation requirements and maintenance of validated status. Lessons learned from EMTCT validation show that dual elimination supports synergies, data verification is challenging, human rights and community engagement issues continue to be important challenges, and sustaining and guarding against complacency once validation is achieved is critical. New approaches to supporting regional review including virtual review are being discussed, following the experience of WPRO for the Malaysia validation of dual elimination of HIV and syphilis. Ultimately, the validation process is country and region-driven and is related to broader HIV and STI programmes and MNCH health systems and the region is uniquely positioned to know the key country issues and provide context-specific technical support.

3.2.2 Proposed impact and programming metrics in Framework for Triple Elimination and validation of HBV EMTCT

Dr Joseph Woodring presented the proposed impact and programming metrics in the Regional framework for the triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis in Asia and the Pacific, 2018-2030 for validation of HBV EMTCT. WHO will establish a coordinated process and mechanisms for validation of EMTCT of HIV, hepatitis B and syphilis. It is anticipated that a country seeking validation of EMTCT of HIV, hepatitis B and/or syphilis will be required to report on a range of impact and programme indicators. A list of indicators, most of which are already being collected by countries, are proposed and may be revised and/or added to as new evidence and recommendations become available. Indicators include policy indicators, impact indicators for HIV, syphilis and HBV and programmatic/process indicators.

The participants divided into two groups for discussions on interventions for EMTCT, and monitoring and assessment of EMTCT.
4. Recommendations

1. Regional action plan: Support Member States to implement the *Regional Action Plan for Viral Hepatitis in the Western Pacific 2016-2020* under universal health coverage, including development of scalable national costed hepatitis action plans, initiating discussions on the next regional action plan, and actively involving people living with hepatitis and civil society.

2. Stigma and discrimination: Support Member States to address stigma and discrimination toward people living with viral hepatitis including monitoring legislation that addresses stigma and discrimination.

3. Advocacy and communication: Support Member States and work with partners and civil society to pursue advocacy and communications to increase public awareness of viral hepatitis including stigma and discrimination, interventions for prevention, testing and treatment of viral hepatitis. Encourage Member States to allocate national resources for advocacy and communications activities. Support countries to develop patient literacy materials and trainings for health-care providers.

4. Prevention: Support Member States to focus on prevention of viral hepatitis through hepatitis B immunization, harm reduction, blood and transfusion safety, and prevention of health care-associated infections. Support Member States to promote approaches for integration of services, including the Regional framework for the triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis in Asia and the Pacific, 2018-2030.

5. Testing: Provide technical support to Member States to adapt WHO guidelines to expand access to quality-assured testing services, including within primary health services. Develop evidence-based testing strategies; facilitate access to affordable quality-assured diagnostics and laboratory services. Disseminate diagnostics pricing data among Member States.

6. Treatment: Support Member States to expand access and linkage from diagnosis to care and treatment services. Facilitate access to medicines and disseminate information on prices. Support training of health-care providers, development of simplified guidelines and decentralized service delivery models, in particular integration of treatment into primary care.

7. Strategic information and progress monitoring: Develop an operational guide providing guidance on data sources that may be used to develop the national cascade of care and monitor impact indicators (i.e. incidence and mortality) and stigma and discrimination. Encourage the inclusion of hepatitis indicators into the national disease surveillance system.

8. Laboratory: Encourage Member States to participate in existing regional laboratory networks and to establish or identify national reference laboratories to support testing capacities. Follow up on recommendations of the Informal Consultation on the Quality Improvement of Laboratory Service for Viral Hepatitis in the Western Pacific Region.

9. Resource mobilization and collaboration: Seek resources to support national hepatitis responses; advocate allocation of national resources for viral hepatitis; expand partnerships and networks, including WHO representation at regional and subregional meetings to provide normative and technical guidance.
10. Other hepatitides: Respond to outbreaks of all forms of hepatitis and provide technical assistance to Member States when requested. Where applicable, support countries to understand the epidemiology of other hepatitides, with particular attention to hepatitis D.

11. Implementation science and evidence generation: Identify priority questions and provide support for implementation research on viral hepatitis to inform policies and decision-making to advance hepatitis response. This may include adaptation and implementation of global recommendations, and integration of hepatitis-related services into existing health systems.

5. Recommendations from the HBV EMTCT

1. EMTCT of HBV: Develop and provide guidance to Member States for interventions, monitoring and assessment of EMTCT of HBV considering the technical recommendations provided through the consultation.

2. Validation of EMTCT: Incorporate the validation process into the existing mechanisms and conduct validation at the regional level as feasible, through active collaboration between ERP/STAC and HIV/syphilis programmes, and cross-cutting collaborations with maternal, newborn and child health and health systems. A standardized assessment scheme should be developed by ERP, STAC and relevant experts.

Technical recommendations and considerations for EMTCT of HBV

1) EMTCT interventions

Key issues for the provision of routine antenatal hepatitis B screening and opportunities for linkages with antenatal HIV and syphilis testing.

Recommendations:
1. Adoption of antenatal HBsAg testing of pregnant women should be in addition to the delivery of the timely birth dose and completion of the hepatitis B vaccine series for all infants, not only those born to HBsAg-positive mothers.
2. Antenatal HBsAg testing should be conducted using a WHO pre-qualified test or a quality-assured test which has been shown independently to have high sensitivity and specificity. If testing is conducted using a rapid test, subsequent confirmatory testing could be considered, if available.
3. Antenatal HBsAg testing should be universally and routinely offered to all pregnant women (together with antenatal HIV and syphilis testing) in both public and private health facilities. Testing should be conducted in every pregnancy at no cost to the individuals.
4. Confidentiality of test results must be ensured and all women should receive counselling and education. Steps must be taken to prevent stigma and discrimination against women living with hepatitis B, both in healthcare settings and in general, including applying lessons learned in the programmatic response to these issues in the context of HIV.
5. Test results must be made available at ANC and at the place of delivery and of postnatal follow-up. Policies supported by standing orders should ensure that healthcare providers in the delivery facility are trained and authorised to give the HepB-BD, to facilitate timely delivery of the HepB-BD.
6. Women identified as HBsAg-positive should be linked to timely and appropriate care and informed of the importance of facility-based delivery, timely HepB-BD for their newborns, completion of the hepatitis B vaccine series and follow-up for themselves and their infant.

7. HBsAg testing should be offered and made available to partners, family and household contacts of HBsAg-positive pregnant women.

8. All women who are diagnosed with hepatitis B antenatally must be entered in the national hepatitis case notification system, including those women who were diagnosed through rapid testing during labour and delivery.

9. Monitoring (data) of mother-baby pairs should be linked, so that the HBsAg status of the mother and the vaccination status of the infant are known.

10. Consideration may be given to offering hepatitis B vaccination to women at risk of hepatitis B infection who remain susceptible to hepatitis B.

11. Countries would need to undertake workforce development to provide appropriate care to HBsAg-positive pregnant women identified through antenatal screening and must ensure proper training of all staff involved in EMTCT, including the use of algorithms and training in the use of antiviral drugs if available.

Minimum intervention package for HBsAg-positive pregnant women and their infants

Recommendations:
The minimum intervention package should include:

1. Timely HepB-BD, given to the infant as soon as possible after birth (and definitely within 24 hours), followed by completion of the hepatitis B vaccine series according to the national immunization schedule.

2. Additional interventions to reduce the risk of MTCT of hepatitis B:
   a. HBIG given to the infant, where available, or
   b. HBIG for the infant and antiviral drugs given to the mother, or
   c. (pending research results) antiviral drugs given to the mother alone.

3. Post vaccination serologic testing (PVST) for infants born to HBsAg-positive mothers and linkage to appropriate care for infants diagnosed with hepatitis B.

4. Counselling and education and linkage to care for infected women (either during pregnancy or postpartum).

5. Promotion of partner/family/household contact testing and linkage to care.

Key issues to be considered for HBIG use

Recommendations:

1. If a country decides to use HBIG as a measure to reduce MTCT of hepatitis B, the quality and safety of HBIG should be ensured through national regulatory, procurement and supply systems.

2. The cost of HBIG should be borne by the programme, not by the individual family.

3. HBsAg-positive women should be encouraged and supported to deliver at the health facility level where HBIG is available to ensure that HBIG can be given in a timely manner.
Key issues to be considered for antiviral use

Recommendations:
1. Tenofovir disoproxil fumarate (TDF) is the preferred drug in the setting of prevention of MTCT of hepatitis B. Before treatment is initiated, testing should be conducted to confirm adequate baseline renal function, in line with national treatment guidelines.
2. HBIG (if available) should be given to the newborns of women who present late in pregnancy, at labour or delivery and are determined to be HBsAg-positive, as antivirals will have insufficient time to work.
3. HIV-HBV co-infected pregnant women should be on a TDF-containing antiretroviral combination regimen.
4. The cost of antiviral treatment should be borne by the programme, not by the individual family.
5. Antivirals should not be stopped at delivery in women who need treatment for their own health. HBsAg-positive mothers should be linked to care during pregnancy and after delivery.
6. Consideration can be given to the use of HBeAg testing where HBV DNA VL testing is not available to indicate need for additional antiviral therapy.
7. If the availability of specialist physicians in-country is limited and antivirals will be prescribed predominantly by primary care physicians, training should be provided in the use of the drugs, monitoring procedures and follow-up.

Follow-up of exposed infants

Recommendations:
1. Post vaccination serologic testing (PVST) of infants for HBsAg should be conducted not less than 2 months after the last dose of hepatitis B vaccine and before 18 months of age, at a time which takes advantage of existing healthcare interventions for the child (for example at the time of measles vaccination i.e. 9 months).
2. The use of WHO pre-qualified tests or tests which have been shown independently to have high sensitivity and specificity is recommended. Approved rapid diagnostic tests can be used if available.
3. At minimum, an HBsAg test should be conducted. If a rapid test is used and the result is positive, confirmatory testing should be conducted if available.
4. Countries may choose to offer anti-HBs testing (in addition to HBsAg testing) if available. Anti-HBs testing should be conducted before 24 months as antibody levels decline with time after vaccination. Infants who are both anti-HBs and HBsAg-negative should be considered for revaccination.
5. Infants found to have HBV infection should be linked to appropriate care.
6. Family and household members should be identified, offered HBsAg testing and vaccination if found to be susceptible.
2) Monitoring and assessment

Metrics of EMTCT of HBV

Recommendations:
1. The metric of EMTCT of HBV is the proportion of babies born to HBsAg-positive women who, at 9-12 months*, are HBsAg-positive.
   *where this timing must satisfy: >2 months since last dose of hepatitis B vaccine and age <18 months

Justification:
- The ~5 year-old prevalence metric (0.1% HBsAg-positive) in the general population reflects overall health system strengthening (HSS)/SDG targets and all prevention efforts (including but not limited to MTCT) and only reflects on MTCT indirectly and after a time-delay.
- This ~5 year-old prevalence metric needs to remain prominent in any EMTCT framework and country report and should be included as an additional overall measure.

2. An MTCT rate of hepatitis B <2% represents EMTCT of HBV

Justification:
- This MTCT rate is achievable, based on available data from Thailand and China which have greater than 95% vaccination coverage, including that of the HepB-BD.
- This MTCT rate is expected to be consistent with the 2030 target of <0.1% HBsAg prevalence among ~5 year-old children.
- This is consistent with the HIV EMTCT target in the region.

Note: this is not eradication, but represents a very low level of risk and a low level public health problem.

Evidence of MTCT rate of HBV <2%

Recommendations:
Packages of data which may constitute an acceptable level of evidence for a MTCT rate of HBV <2% include:
1. A nationally representative prospective cohort of HBsAg-positive mothers and their babies followed to 12 months of age, with high levels of follow-up.
2. A high quality estimate of MTCT using routine programmatic data, such as a retrospective cohort of HBsAg-positive, mothers´ census or a nationally representative sample (including >90% capture of ANC events; >90% ascertainment of mother´s HBsAg status; and >90% of ascertainment of child´s outcome). [Metrics TBD]
3. A high quality estimate of MTCT using routine programmatic data supplemented with active follow-up and testing of a representative sample of hepatitis B-exposed infants at 9-12 months to improve ascertainment. [Metrics TBD]
4. Triangulation of more than one estimate as described above, where data packages include moderate limitations.

Additional modelling estimates of MTCT based on high-quality programme service coverage data, including mothers tested, maternal HBsAg seroprevalence, mothers treated, newborn and infant vaccines, etc. would be useful particularly where data sources are limited.

Note: data packages 1-3 are the preferred methodologies
The role of modelling in judging achievement of EMTCT:
1. Contributes to the evidence base for the MTCT rate of hepatitis B - but not in isolation.
2. Helps design data collection/analysis to measure the MTCT rate of hepatitis B.
3. Provides ‘consistency’ checks for data.

Notes:
- Models should be peer-reviewed, of high quality and with demonstrated validity for the setting and application.
- There may be a role for comparing outputs from more than one model (currently, there is no hepatitis B consensus model such as Spectrum for HIV).

The role and details of programme data in validation of EMTCT of HBV

Recommendations:
1. Every evaluation of EMTCT should incorporate programme data and should include ANC attendance and screening, timely birth dose coverage, HB3 coverage, HBIG uptake, linkage to care and treatment for HBsAg-positive mothers, antivirals (when available) and PVST coverage and outcome for infants.
2. Estimates should be population-based and consider women who have not been captured by the system.
3. Programme data from multiple sources should be triangulated; this can be through modelling.

Note: the above indicators need to be further defined

Validation of EMTCT of HBV

Recommendations:
1. ERP and external experts should assist countries by providing guidance on what is required for validation.
2. The validation process should be transparent and in partnership with countries.
3. Countries should be encouraged to undergo validation of EMTCT for HBV, HIV and syphilis in combination, where feasible.
4. The validation process should be incorporated into existing mechanisms (e.g. ERP), and should mirror how progress towards elimination is currently reviewed by country.
5. The validation process should be led by ERP but must incorporate external experts and be done in collaboration with HIV and syphilis, MNCH and health systems experts and groups.
6. A new standardised marking scheme should be developed to assess EMTCT by the ERP, STAC and relevant experts, and should include assessment of indicators (programme data), MTCT rate and modelling.

Working across existing regional and global validation systems

Recommendations:
1. Regional
   - There should be active collaboration between ERP/STAC and HIV/syphilis groups, and cross-cutting collaborations with MNCH and health systems, such as formation of joint working groups.
   - Validation should be conducted at the regional level, where feasible.
2. Global
   • Global and regional validation activities should be aligned.
   • Revision of the “orange book for triple EMTCT” to include validation of EMTCT of hepatitis B should draw on regional and national expertise and experience
ANNEX 1: Provisional List of Participants, Temporary Advisers, Representatives/Observers and Secretariat

1. Participants

**China**

**WANG Fuzhen**, Researcher/Professor, Chinese Center for Disease Control and Prevention, Beijing, Tel: 86-1083133797, E-mail: wangfz@chinacdc.cn

**ZHENG Hui**, Associate Researcher, Chinese Center for Disease Control and Prevention, Beijing, Tel: 86-1083133797, E-mail: zhenghui@chinacdc.cn

**Malaysia**

**ANITA Suleiman**, Consultant Public Health Physician, Head of Sector HIV/STI/HEPATITIS C, Ministry of Health Malaysia, Federal Government Administrative Centre, Putrajaya, Tel: +603 88834262, Fax: +603 88834285, E-mail: dranita@moh.gov.my

**A'AISAH Senin**, Head of Sector, Vaccine Preventable/Food and Waterborne Disease, Disease Control Division, Ministry of Health Malaysia, Federal Government Administrative Centre, Putrajaya, Tel: +601 93312382 / +603 88834411, Fax: +603 88891013, E-mail: aaisah@moh.gov.my

**Rozita AB RAHMAN**, Public Health Physician, EPI Manager, Family Health Development Division, Ministry of Health Malaysia, Federal Government Administrative Centre, Putrajaya, Tel: +603 88834042, Fax: +603 88886175, E-mail: drrozita.ar@moh.gov.my

2. Temporary Advisers

**ERP Members**

**Benjamin COWIE**, Epidemiologist Physician, Victorian Infectious Diseases Reference Laboratory, Wreckyn Street, North Melbourne, Victoria 3051, Australia, Tel: (61-3) 93422606, Fax: (61-3) 93422666, E-mail: Benjamin.Cowie@mh.org.au

**Dambadarjaa DAVAALKHAM**, Head, Department of Epidemiology and Biostatistics, Health Sciences University, Ulaanbaatar, Mongolia, Tel: (976-11) 99090141, Fax: (976-11) 321249, E-mail: davaalham@yahoo.com

**Cui FUQIANG**, Professor and Head, Department of Laboratory Science and Technology, School for Public Health, Peking University, No. 38, Xueyuan Road, Beijing, Tel: +86-10-82801518, E-mail: cuifuq@126.com

**Youngmee JEE**, Director General, Center for Infectious Disease Research, National Center for Disease Control and Prevention, Osong, Cheongju, Chungcheongbuk-do, Republic of Korea, Tel: +82 43 719 8400, E-mail: jeey62@gmail.com, jeey@korea.kr

**Mark KANE**, Consultant on Immunization Policy, 4816 West Mercer Way, Washington 98040, United States of America, Tel no: 1-206 2752983, Email: mark.a.kane@gmail.com
Eric MAST, Associate Director for Science, Global Immunization Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Atlanta, GA 30333, United States of America, Tel: 1 404 639 7862, Fax: 1 404 639 8573, E-mail: emast@cdc.gov

Tilman RUFF, Associate Professor, Nossal Institute for Global Health, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Melbourne, Australia, Tel: (613) 9592 8643, Fax: (613) 9692 4682, E-mail: tar@unimelb.edu.au

Takaji WAKITA, Director, Department of Virology II, National Institute of Infectious Diseases (NIID), 1-23-1, Toyama, Shinjuku, Tokyo 162-8640, Japan, Tel: (813) 5185 1111 ext 2500, Fax: (813) 5185 1161, E-mail: wakita@nih.go.jp

John WARD, Director, Program for Viral Hepatitis Elimination, The Task Force for Global Health, Senior Scientist, National Center for HIV/AIDS, Viral Hepatitis, STD, 330 West Ponce de Leon Ave., Decatur, Georgia 30030, United States of America, Tel: +1 404 7367325, E-mail: jward@taskforce.org

STAC Members

CHAN Henry Lik Yuen, Professor, Department of Medicine and Therapeutics, Director, Centre for Liver Health, The Chinese University of Hong Kong, Hong Kong, Prince of Wales Hospital, Shatin, N.T., Hong Kong, China, E-mail: hlychan@cuhk.edu.hk

Kathleen JACKSON, Senior Scientist, Research & Molecular Development, Victorian Infectious Diseases Reference, Laboratory, Melbourne, Australia, Tel: + 81 3 9342 9637, E-mail: Kathy.Jackson@vidrl.org.au

Tatsuya KANTO, Chief Division of Advanced Medical, Therapy for Liver Diseases, The Research Center for Hepatitis and Immunology, National Center for Global Health and Medicine, 1-7-1, Kohnodai, Ichikawa, 272-8516, Japan, Tel: (81)47 372 3501, E-mail: kantotatsuya@gmail.com

WEI Lai, Professor, Department of Pathology and Medicine, Peking University People’s Hospital, Peking University, Hepatology Institute in Beijing, Xicheng district, Beijing, People’s People's Republic of China, Tel: 8610 88325730, E-mail: weilai@pkuph.edu.cn

Rosmawati MOHAMED, Consultant Hepatologist, University Malaya Medical Center, Kuala Lumpur, Malaysia, Tel: +60 3 794 92867, Fax: +60 3 795 56936, E-mail: ros@ummc.edu.my

Michael NINBURG, President of the Executive Board, World Hepatitis Alliance, 7 Rue du Marche, 1204 Geneva, Switzerland, Tel: +41 22 518 06 16, Email: mhninburg@hepeducation.org

Janus ONG, Hepatology Society of the Philippines, Clinical Associate Professor, UP College of Medicine, Ermita, Manila, Philippines, Tel: +632 964 3294, Email: janus.ong@gmail.com

Samuel SO, Director, Asian Liver Center, 780 Welch Ave., C130, Palo Alto, CA 94304, United States of America, Tel: +1650 4986092, Fax: +1650 7361048, Email: samso@stanford.edu
3. Resource Persons

Francisco AVERHOFF, Deputy Director, Global Health Division of Viral Hepatitis, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, E-mail: fma0@cdc.gov

Timothy HALLETT, Professor, Department of Infectious Disease Epidemiology, Imperial College, London, United Kingdom, Tel: +44 (0) 20 7594 1150, E-mail: timothy.hallett@imperial.ac.uk

HOU Jin-Lin, Director, SHIELD zero transmission of HBV project, Nanfang Hospital, South Medical University, Guangzhou, China, Tel: +86 020 61641941, Email: jihousmu@163.com

Elizabeth MASON, Independent Consultant, Putney Hill, London, United Kingdom, Tel: +447539584181, E-mail: masonelizabeth108@gmail.com

Giten KHWAIRAKPAM, Project Manager for Community and Policy, TREAT Asia, Exchange Tower, 388 Sukhumvit Road, Suite 2104, Klongtoey, Bangkok 10110, Thailand, Tel: +662 6637561, E-mail: giten.khwairakpam@treatasia.org

Nathan SHAFFER, Co-chair, Global Validation Advisory Committee on elimination of mother-to-child transmission of HIV and syphilis (consultant), 215 Lamont Drive, Decatur, Georgia 30030, United States of America, Tel: +1 404 747 6238, Email: shaffer.nathan@gmail.com

Rania TOHME, Team Lead, Targeted Vaccine Preventable Diseases, Accelerated Disease Control, and VPD Surveillance Branch, Global Immunization Division, Centers for Disease Control and Prevention, Mailstop E98, 1600 Clifton Road NE, Atlanta, GA 30329, United States of America, Tel: (1-404) 7188577, Fax: (1-404) 4718456, E-mail: ihb1@cdc.gov

Christian TREPO, Fondation Mérieux, 17 rue Bourgelat, 69002 Lyon, France, Tel: +33 472 40 7979, Fax: +33 472 40 7950, E-mail: ctrepo@hotmail.com

ZHANG Lei, Monash University (Australia), School of Public Health and Preventive Medicine, Melbourne, Australia, Tel: +61 (2) 9385 0875, E-mail: Lzhang@kirby.unsw.edu.au

4. Observers

LIU Zhihua, Professor & Attending Physician, Department of Infectious Diseases, Nanfang Hospital, Southern Medical University, Guangzhou, 510515, Tel: +86-20-62787312, E-mail: zhihualiu@126.com

Masamichi MURAMATSU, Director, Department of Virology II, National Institute of Infectious Diseases, 1-23-1 Toyama, Shinjuku Tokyo 162-8640, Japan, Tel: 632 5363642, E-mail: muramatsu@nih.go.jp

Nicole ROMERO, Epidemiologist, Peter Doherty Institute for Infection and Immunity, WHO Collaborating Centre for Viral Hepatitis, Melbourne, Australia, Tel: 0451 195 211, E-mail: nicole.romero7@gmail.com

Olivier SEGERAL, International Technical Expert and Assistant, French Agency for Research on AIDS and Viral Hepatitis, University of Health Sciences, Phnom Pehn, Cambodia, Tel: +855 12 479 313, Email: oliseg@hotmail.com
5. Secretariat

WHO/WPRO

Naoko ISHIKAWA. Coordinator, HIV, Hepatitis and STI, WHO Regional Office for the Western Pacific, P.O. Box 2932, 1000 Manila, Philippines, Tel: (632) 528 9714, Fax: (632) 521 1036, E-mail: ishikawan@who.int

Yoshihiro TAKASHIMA. Coordinator, Expanded Programme on Immunization, WHO Regional Office for the Western Pacific, P.O. Box 2932, 1000 Manila, Philippines, Tel: (632) 528 9746, Fax: (632) 521 1036, E-mail: takashimay@who.int

Po-Lin CHAN. Medical Officer, HIV, Hepatitis and STI, WHO Regional Office for the Western Pacific, P.O. Box 2932, 1000 Manila, Philippines, Tel: (632) 528 9750, Fax: (632) 521 1036, E-mail: chanpo@who.int

Joseph WOODRING. Technical Officer (Hepatitis B Control and Prevention), Expanded Programme on Immunization, WHO Regional Office for the Western Pacific, P.O. Box 2932, 1000 Manila, Philippines, Tel: (632) 528 9037, Fax: (632) 521 1036, E-mail: woodringj@who.int

Linh-vi LE. Epidemiologist, HIV, Hepatitis and STI, WHO Regional Office for the Western Pacific, P.O. Box 2932, 1000 Manila, Philippines, Tel: (632) 528 9711, Fax: (632) 521 1036, E-mail: leli@who.int

Donghyok KWON. Technical Officer, HIV, Hepatitis and STI, WHO Regional Office for the Western Pacific, P.O. Box 2932, 1000 Manila, Philippines, Tel: (632) 528 9718, Fax: (632) 521 1036, E-mail: kwond@who.int

Takeshi NISHIJIMA. WHO GO Special Fellow, HIV, Hepatitis and STI, WHO Regional Office for the Western Pacific, P.O. Box 2932, 1000 Manila, Philippines, Tel: (632) 528 9716, Fax: (632) 521 1036, E-mail: nishijimat@who.int

James HEFFELFINGER. Technical Officer, New Vaccines, Expanded Programme on Immunization, WHO Regional Office for the Western Pacific, P.O. Box 2932, 1000 Manila, Philippines, Tel: (632) 528 9033, Fax: (632) 521 1036, E-mail: heffelfingerj@who.int

WHO/Headquarters

Marc BULTERYS. Team Leader, Global Hepatitis Programme, World Health Organization, Geneva, Switzerland, Tel: +41 22 791 4454, E-mail: bulterysm@who.int

WHO/PHL

Nerissa DOMINGUEZ. National Professional Officer, HIV, Hepatitis and STI, WHO Office in the Philippines, Department of Health, San Lazaro Compound, Rizal Avenue, Sta Cruz, Manila, Philippines, Tel: (632) 310 6370, E-mail: dominguezn@who.int
## ANNEX 2: Meeting Agenda

**THIRD STRATEGIC AND TECHNICAL ADVISORY COMMITTEE (STAC) FOR VIRAL HEPATITIS AND SIXTH HEPATITIS B IMMUNIZATION EXPERT RESOURCE PANEL (ERP) JOINT CONSULTATION**  
Manila, Philippines, 17-20 September 2018

**Meeting agenda**  
**Version 6.5**

### Day 1: 17 September 2018

<table>
<thead>
<tr>
<th>Time</th>
<th>STAC and ERP Combined Sessions (in Conference Hall)</th>
<th>Speaker/Moderator</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:30-09:00</td>
<td>Registration</td>
<td></td>
</tr>
</tbody>
</table>
| 09:00-09:30    | **Opening**  
|                |  
|                |   - Welcome remarks                                                                                                 | Naoko Ishikawa and Yoshihiro Takashima                |
|                |   - Opening remarks                                                                                                  | Mark Jacobs                                            |
|                |   - Self-introduction and objectives of the consultation                                                            | Po-Lin Chan and Joseph Woodring                        |
|                |   - Administrative announcements                                                                                     |                                                       |
| 09:30-10:00    | **Group photo and coffee break**                                                                                     | Moderator: Takaji Wakita/ Rosmawati Mohamed            |
| 10:00-10:20    | **Global overview**  
|                |   - HBV prevention and progress towards elimination of viral hepatitis (GHP and IVB joint presentation)               | Marc Bulterys                                          |
| 10:20-11:00    | **Regional overview (10 min each)**  
|                |   - Progress of hepatitis B control through immunization in the Western Pacific                                     | Joseph Woodring                                        |
|                |   - Regional Action Plan for Viral Hepatitis in the WPR2016-2020 implementation progress                          | Po-Lin Chan                                            |
|                | **EMTCT of HIV, hepatitis B and syphilis: an opportunity to further**                                               | Naoko Ishikawa                                         |
### 11:00-12:00
Advance accelerated hepatitis B control

Country experiences – eliminating viral hepatitis (15 min each)
- China – EMTCT of HBV
- Malaysia – Hepatitis B and C elimination

Discussion

<table>
<thead>
<tr>
<th>Time</th>
<th>STAC (in Room 210)</th>
<th>Speaker/Moderator</th>
<th>Time</th>
<th>ERP (in Room 212)</th>
<th>Speaker/Moderator</th>
</tr>
</thead>
<tbody>
<tr>
<td>13:00-13:10</td>
<td>Review of previous STAC recommendations</td>
<td>Naoko Ishikawa</td>
<td>13:00-13:15</td>
<td>Regional EPI update</td>
<td>Moderator: Takaji Wakita</td>
</tr>
<tr>
<td>13:40-13:50</td>
<td>Promoting testing: Finding the missing millions</td>
<td>Giten Khwairakpam</td>
<td>13:45-14:00</td>
<td>Countries with recently completed or planned serosurveys</td>
<td>Rania Tohme</td>
</tr>
</tbody>
</table>

12:00-13:00 Lunch

### 12:00-13:00
Lunch
<table>
<thead>
<tr>
<th>Time</th>
<th>Session Title</th>
<th>Speaker</th>
<th>Time</th>
<th>Session Title</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>13:50-14:00</td>
<td>Elimination of hepatitis in Japan: prevention and treatment beyond general population to reach the Unreached</td>
<td>Tatsuya Kanto</td>
<td>14:15-14:30</td>
<td>Utilizing templated protocols for biomarker serosurveys</td>
<td>Marc Bulterys</td>
</tr>
<tr>
<td>14:00-15:00</td>
<td>Discussion: priority actions [Key questions]</td>
<td></td>
<td>14:30-14:45</td>
<td>Progress of sampling in low seroprevalence target groups</td>
<td>Rania Tohme</td>
</tr>
<tr>
<td>15:00-15:30</td>
<td>Coffee break</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15:30-15:50</td>
<td>Health systems and viral hepatitis</td>
<td>Peter Cowley</td>
<td>15:30-15:50</td>
<td>Report from the Informal Consultation on the Quality Improvement of Laboratory Service for Viral Hepatitis</td>
<td>Donghyok Kwon</td>
</tr>
<tr>
<td>15:50-16:00</td>
<td>Discussion (10 min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16:00-16:20</td>
<td>Laboratory services for hepatitis - report from the Informal Consultation on the Quality Improvement of Laboratory Service for Viral Hepatitis</td>
<td>Donghyok Kwon</td>
<td>15:50-16:10</td>
<td>Findings from the Viral Hepatitis Board Meeting</td>
<td>John Ward</td>
</tr>
<tr>
<td>16:20-16:30</td>
<td>Discussion (10 min)</td>
<td></td>
<td>16:10-16:30</td>
<td>Regional progress in healthcare workers programmes for hepatitis B vaccination</td>
<td>Joseph Woodring</td>
</tr>
<tr>
<td>16:30-16:45</td>
<td>Global reporting and strategic information for viral hepatitis</td>
<td>Linh-Vi Le</td>
<td>16:30-17:00</td>
<td>Discussion</td>
<td></td>
</tr>
<tr>
<td>16:45-17:00</td>
<td>Discussion (15 min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17:00-17:30</td>
<td>Secretariat meeting</td>
<td></td>
<td>17:00-17:30</td>
<td>Secretariat meeting</td>
<td></td>
</tr>
<tr>
<td>17:30-19:00</td>
<td>Regional Director's Reception</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Day 2: 18 September 2018

<table>
<thead>
<tr>
<th>Time</th>
<th>STAC (in Room 210)</th>
<th>Speaker/Moderator</th>
<th>Time</th>
<th>ERP (in Room 212)</th>
<th>Speaker/Moderator</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:00-09:30</td>
<td>Estimating burden of disease and cascade of care – modeling and programmatic data</td>
<td>Ben Cowie &amp; Homie Razavi (by teleconference)</td>
<td>09:00-09:15</td>
<td>Scaling up Outside of Cold Chain activities in the Solomon Islands</td>
<td>Joseph Woodring</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>09:15-09:30</td>
<td>Birth dose improvement activities in Viet Nam</td>
<td>Joseph Woodring</td>
</tr>
<tr>
<td>09:30-10:00</td>
<td>Discussion: priority actions [Key questions]</td>
<td></td>
<td>09:30-09:45</td>
<td>China’s work towards elimination of hepatitis B virus</td>
<td>Fuqiang Cui</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>09:45-10:00</td>
<td>Discussion</td>
<td></td>
</tr>
<tr>
<td>10:00-10:30</td>
<td>Coffee break</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10:30-11:30</td>
<td>Recommendations and next steps</td>
<td></td>
<td>10:30-11:00</td>
<td>Priority activities for 2018-2020 and 2021-2030</td>
<td>Eric Mast</td>
</tr>
<tr>
<td>11:30-12:00</td>
<td>STAC – review of the TOR, election of new chairs and STAC’s way of working</td>
<td></td>
<td>11:00-12:00</td>
<td>Formulation of ERP recommendations and next steps</td>
<td>Takaji Wakita</td>
</tr>
<tr>
<td>12:00-13:00</td>
<td>Lunch break</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td>STAC and ERP Combined Sessions (in Conference Hall)</td>
<td>Speaker/Moderator: Takaji Wakita/ Rosmawati Mohammad</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13:00-13:15</td>
<td>Maternal, newborn and child health (MNCH) and viral hepatitis</td>
<td>Fuqiang Cui</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13:15-13:30</td>
<td>Fostering collaborations among MNCH, EPI and HSI</td>
<td>Timothy Hallett</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13:30-13:45</td>
<td>EMTCT HBV modelling in China</td>
<td>Lei Zhang</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13:45-14:00</td>
<td>Cost effective analysis of triple elimination in Cambodia</td>
<td>Samuel So</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Communication activities for hepatitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Healthcare associated infections</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14:00-14:15</td>
<td>Developing a healthcare worker vaccination programme in China</td>
<td>Fuqiang Cui</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14:15-14:30</td>
<td>Preventing healthcare associated infections and vaccination for healthcare workers</td>
<td>Benjamin Cowie</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14:30-15:00</td>
<td>Discussion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15:00-15:30</td>
<td>Coffee break</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15:30-16:00</td>
<td>Report from ERP and STAC Chairs (15 min each)</td>
<td>Takaji Wakita &amp; Henry Chan</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16:00-16:30</td>
<td>Joint recommendations – discussion</td>
<td>Facilitated discussion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16:30-17:00</td>
<td>Closing session</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adjournment of ERP and STAC Meetings
**Elimination of mother-to-child transmission of HBV: interventions, criteria and process of validation**

Day 3: 19 September 2018

<table>
<thead>
<tr>
<th>Time</th>
<th>Topic</th>
<th>Presenter/facilitator</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:00 – 09:10</td>
<td>Opening and objectives of the meeting (in Room 210)</td>
<td>Naoko Ishikawa</td>
</tr>
<tr>
<td>09:10 – 10:30</td>
<td><strong>Session 1: Understanding evidence for EMTCT of HBV</strong></td>
<td>Naoko Ishikawa</td>
</tr>
<tr>
<td></td>
<td>1) Interventions for EMTCT – antenatal screening and use of HBIG, antivirals and post-vaccination serologic testing (PVST)</td>
<td>Marc Bulterys</td>
</tr>
<tr>
<td></td>
<td>- Current evidence and research findings on EMTCT HBV interventions (15 min)</td>
<td>Jin-Lin Hou</td>
</tr>
<tr>
<td></td>
<td>- Preliminary findings from ongoing studies (10 min each)</td>
<td>Olivier Segeral</td>
</tr>
<tr>
<td></td>
<td>SHIELD zero transmission HBV EMTCT project, China</td>
<td>Nicole Romero</td>
</tr>
<tr>
<td></td>
<td>Pragmatic HBIG-free regimen: ANRSTA PROHM Cambodia</td>
<td>WPRO</td>
</tr>
<tr>
<td></td>
<td>Victoria Perinatal HBV prevention project, Australia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Existing guidance for EMTCT interventions of HBV in countries (10 min)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Discussion</td>
<td></td>
</tr>
<tr>
<td>10:30 – 11:00</td>
<td><strong>Tea break</strong></td>
<td></td>
</tr>
<tr>
<td>11:00 -12:30</td>
<td>2) Assessment and validation of EMTCT (15 min each)</td>
<td>Nathan Shaffer</td>
</tr>
<tr>
<td></td>
<td>- Lessons learned from validation of HIV and syphilis</td>
<td>WPRO</td>
</tr>
<tr>
<td></td>
<td>- Proposed impact and programming metrics in Framework for Triple Elimination and validation of HBV EMTCT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Discussion</td>
<td></td>
</tr>
<tr>
<td>Time</td>
<td>Activity</td>
<td>Facilitators</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------------------------------------------------------------------</td>
<td>-------------------------------------</td>
</tr>
<tr>
<td>12:30-13:30</td>
<td>Lunch break</td>
<td></td>
</tr>
<tr>
<td>13:30 – 16:30</td>
<td>Session 2: Developing draft regional operational document (group work)</td>
<td>WPRO</td>
</tr>
<tr>
<td></td>
<td>Introduction to the group work</td>
<td>Benjamin Cowie/ Elizabeth Mason</td>
</tr>
<tr>
<td></td>
<td>Group A: Interventions for EMTCT (Room 210)</td>
<td>Nathan Shaffer/ Timothy Hallett</td>
</tr>
<tr>
<td></td>
<td>Group B: Monitoring and assessment of EMTCT (Room 212)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Each group will present group findings on 20 September, including draft</td>
<td></td>
</tr>
<tr>
<td></td>
<td>operational guidelines.</td>
<td></td>
</tr>
</tbody>
</table>

Day 4: 20 September 2018

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Facilitators</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00 – 11:30</td>
<td>Session 2: Developing operational document (continued)</td>
<td>WPRO</td>
</tr>
<tr>
<td></td>
<td>Group A: Interventions for EMTCT (Room 210)</td>
<td>Benjamin Cowie/ Elizabeth Mason</td>
</tr>
<tr>
<td></td>
<td>Group B: Monitoring and assessment of EMTCT (Room 212) Lunch break</td>
<td>Nathan Shaffer/ Timothy Hallett</td>
</tr>
<tr>
<td>11:30 – 13:00</td>
<td>Lunch break</td>
<td></td>
</tr>
<tr>
<td>13:00 – 15:00</td>
<td>Session 3: summary and recommendations (Room 210)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Presentation from group work (15 min each)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Discussion and conclusion</td>
<td></td>
</tr>
<tr>
<td>15:00</td>
<td>Closing</td>
<td></td>
</tr>
</tbody>
</table>