



WHO

# Hepatitis B Control Through Immunization: A Reference Guide



World Health  
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Western Pacific Region





# **Hepatitis B Control Through Immunization: A Reference Guide**

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# ABBREVIATIONS

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AEFI	adverse event following immunization
Anti-HBs	antibodies to hepatitis B surface antigen
Anti-HBc	antibodies to hepatitis B core antigen
CTC	controlled temperature chain
DPT	diphtheria-pertussis-tetanus vaccine
ELISA	enzyme - linked immunosorbent assay
EPI	Expanded Programme on Immunization
ERP	Hepatitis B Expert Resource Panel
HBcAg	hepatitis B core antigen
HBeAg	hepatitis B 'e' antigen
HBIG	hepatitis B immunoglobulin
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HepB	hepatitis B vaccine
Hib	Haemophilus influenzae type B
RED	Reaching Every District
TAG	Technical Advisory Group
UNICEF	United Nations Children's Fund
US CDC	United States Centers for Disease Control and Prevention
VVM	vaccine vial monitor

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# FOREWORD

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Hepatitis B prevention and control is a high priority for me as the World Health Organization Regional Director for the Western Pacific — the Region which has historically had the highest hepatitis B burden.

Hepatitis B infection causes deadly cirrhosis and cancer of the liver. The best protection from this deadly virus is three doses of vaccine in infancy, with the first dose administered within 24 hours of birth. Extremely safe and effective, the vaccine is the best tool we have for protecting children.

Member States have prioritized hepatitis B vaccination. Now millions of infants receive the complete series every year, and hepatitis B infection among infants and children has fallen dramatically, and continues to decline.

Indeed, the success of the Western Pacific Region has been remarkable. Since 2003, 10 million chronic hepatitis B infections have been prevented in the Region, saving an estimated 2.5 million people from hepatitis B-related deaths.

This milestone is the result of national actions to control hepatitis B. By 2012, 30 countries and areas in the Region had reduced prevalence among children to less than 2% — compared to prevalence rates higher than 6% in the pre-vaccine era.

In October 2013, the Regional Committee for the Western Pacific passed a resolution to further reduce hepatitis B — to less than 1% chronic infection prevalence among children by 2017.

This latest goal will save millions more in the Region from the devastating effects of hepatitis B.

To support Member State efforts to reach this goal, I am pleased to introduce *Hepatitis B Control Through Immunization: A Reference Guide*, which provides guidance and targets for hepatitis B control.

The Western Pacific Region was the first to establish a hepatitis B control goal. With close cooperation and strong government leadership, the Region can also become the first to reduce the disease's deadly toll to historic lows.

As always, I welcome the opportunity to work with each Member State towards the achievement of our shared goal.



ShinYoung-soo, MD, Ph.D.  
Regional Director for the Western Pacific  
World Health Organization

# SUMMARY

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*Hepatitis B Control Through Immunization: A Reference Guide* is intended to provide a handy compilation of available guidance for hepatitis B vaccination programs in countries and areas of the Western Pacific Region. The Western Pacific Region, despite being home to approximately 28% of the global population, bears a disproportionate burden of hepatitis B virus (HBV)-related mortality and morbidity, accounting for almost half of all chronic hepatitis B infections worldwide.<sup>1</sup> With an estimated 160 million chronic HBV carriers living in the Region, hepatitis B is responsible for nearly 900 deaths per day, a mortality rate comparable to that of tuberculosis.<sup>1</sup> Most countries had a chronic HBV infection rate of more than 10% before the introduction of vaccination.<sup>2</sup> Of the 325 000 estimated annual deaths caused by HBV infection in the Region, nearly all are consequences of chronic infection, mostly decades after the initial infection at birth or in early childhood. Hepatitis B, therefore, is an important regional public health priority.

Universal childhood immunization with three doses of hepatitis B vaccine in the first year of life has been proven to be the most effective strategy for the prevention and control of hepatitis B. In 2005, the Western Pacific Region achieved the distinction of being the first WHO region to incorporate infant hepatitis B immunization in the national immunization programmes of all its Member States.

In 2003, the fifty-fourth session of the WHO Regional Committee for the Western Pacific set a goal to reduce the prevalence of chronic hepatitis B infection among 5-year-old children to less than 1% (WPR/RC54.R3) in 2005 an interim milestone of reducing chronic HBV infection among children to less than 2% by 2012 was established (WPR/RC64.R5). By 2012, the Region as a whole and 30 countries and areas were estimated to have met the milestone. Striving to build upon these gains, in 2013, the sixty-fourth session of the WHO Regional Committee for the Western Pacific has now resolved to meet the goal of reducing chronic HBV infection to less than 1% among 5-year-old children by 2017 (WPR/RC64.R5). Achievement of this goal will translate to an additional 60 000 hepatitis B-related deaths averted per birth cohort in the Region.

There are five key strategic areas for hepatitis B prevention through vaccination.

## 1. Vaccination of infants

- Strengthening of routine immunization services to achieve and sustain at least 95% coverage with three doses of hepatitis B vaccine by 1 year of age in each birth cohort at the national level, and at least 85% coverage in each district.
- Delivery of a timely birth dose (within 24 hours of birth), with a target of reaching at least 95% of births at the national level and at least 85% coverage in each district.
- Coordination with maternal and child health programmes to improve access to immunization and other neonatal care interventions for births outside of health facilities.

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1 Goldstein ST, Zhou F, Hadler SC, Bell BP, Mast EE, Margolis HS. A mathematical model to estimate global hepatitis B disease burden and vaccination impact. *Int J Epidemiol.* 2005;34:1329–39.

2 Rani M, Yang B, Nesbit R. Hepatitis B control by 2012 in the WHO Western Pacific Region: rationale and implications. *Bull World Health Organ.* 2009;87:707–13.

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**Universal childhood immunization with three doses of hepatitis B vaccine in the first year of life has been proven to be the most effective strategy for the prevention and control of hepatitis B.**



## **2. Vaccination of priority adult population groups**

- Immunization of high-risk population groups including health workers, men who have sex with men, sex workers, people who inject drugs, frequent recipients of blood/plasma transfusions, and any other population groups coming in regular contact with blood and blood products.
- Advocacy of national policies requiring free and universal hepatitis B vaccination of health-care workers.

## **3. Vaccine supply and quality**

- Elimination of vaccine stock-outs at the national and district levels through improved training in vaccine management.
- Prevention of vaccine freezing through improved training in temperature monitoring.
- Promotion of use of controlled temperature chain for delivery of hepatitis B birth dose.

## **4. Advocacy and social mobilization**

- Increasing awareness among decision-makers, health workers and caretakers of the risks and consequences of HBV infection and the need for hepatitis B vaccination through:
  - community and civil society engagement,
  - use of media outlets,
  - education materials, and
  - mass awareness campaigns such as World Hepatitis Day and World Immunization Week.

## **5. Measurement of programme performance and impact**

- Measurement of programme performance through monitoring of immunization coverage rates, including establishment of systems to monitor hepatitis B birth dose coverage at the district level.
- Impact measurement through hepatitis B surface antigen (HBsAg) seroprevalence surveys.
- Verification.





# 1. INTRODUCTION

## 1.1 PURPOSE AND FOCUS

The Western Pacific Region, despite being home to approximately 28% of the global population, bears a disproportionate burden of HBV-related mortality and morbidity, accounting for almost half of all chronic hepatitis B infections worldwide.<sup>3</sup> With an estimated 160 million chronic HBV carriers living in the Region, hepatitis B is responsible for nearly 900 deaths per day, a mortality rate comparable to that of tuberculosis.<sup>4</sup> Most countries had a chronic HBV infection rate of more than 10% before the introduction of vaccination.<sup>5</sup> Of the 325 000 estimated annual deaths caused by HBV infection in the Region, nearly all were consequences of chronic infection, mostly decades after the initial infection at birth or in early childhood. Hepatitis B, therefore, is an important regional public health priority.

Striving to build upon the gains achieved in immunization systems during the poliomyelitis eradication initiative, the Western Pacific Region has adopted hepatitis B control through immunization as one of the pillars for strengthening immunization service delivery systems. In 2005, the WHO Regional Committee for the Western Pacific established an interim milestone of reducing chronic HBV infection prevalence to less than 2% among children aged 5 years old by 2012, with a future goal of reaching less than 1% infection prevalence in the Region.<sup>6</sup> The Region as a whole and 30 countries and areas achieved the milestone of less than 2% prevalence by 2012, a remarkable achievement in a region with a disproportionately high burden from hepatitis B. Based on this success, in October 2013, the Regional Committee resolved to meet the goal of reducing chronic HBV infection to less than 1% prevalence in 5-year-old children by 2017.

Since the 2007 hepatitis B regional plan was developed, the hepatitis B programme has reached a new level of maturity, most notably: hepatitis B vaccination has been introduced nationwide across the Region for more than five years; the three-dose series of hepatitis B is provided as part of a combined diphtheria–pertussis–tetanus (DPT) vaccine in the majority of countries; and hepatitis B surface antigen (HBsAg) prevalence among children has decreased dramatically. In addition, the target year for meeting the goal has been set for 2017. As of January 2014, 11 countries and areas have been verified as having achieved the goal of less than 1% HBsAg prevalence among 5-year-old children. In light of these developments, in 2013, the Technical Advisory Group (TAG) on Immunization and Vaccine-Preventable Diseases in the Western Pacific Region recommended updating the hepatitis B regional guidance to reflect the current status of the programme.

This regional reference guide for hepatitis B synthesizes WHO guidance documents published since the last plan was released, namely: *Guidelines for certification of achievement of hepatitis B control goal in the Western Pacific Region*,<sup>7</sup> an updated WHO position paper on hepatitis B vaccination (2009),<sup>8</sup> a WHO review of practices to improve birthdose coverage (2013) and a regional WHO guidance document on vaccination of health-care workers (2013).<sup>9</sup> This new guide also incorporates the recommendations made by TAG during its

**The Region as a whole and at least 30 countries and areas achieved the milestone of less than 2% prevalence by 2012.**

3 Goldstein ST, Zhou F, Hadler SC, Bell BP, Mast EE, Margolis HS. A mathematical model to estimate global hepatitis B disease burden and vaccination impact. *Int J Epidemiol*. 2005;34:1329–39.

4 Rani M, Yang B, Nesbit R. Hepatitis B control by 2012 in the WHO Western Pacific Region: rationale and implications. *Bull World Health Organ*. 2009;87:707–13.

5 Clements CJ, Baoping Y, Crouch A, Hipgrave D, Mansoor O, Nelson CB, et al. Progress in the control of hepatitis B infection in the Western Pacific Region. *Vaccine*. 2006;24:1975–82.

6 Measles elimination, hepatitis B control and poliomyelitis eradication. Manila: World Health Organization Regional Office for the Western Pacific; 2005 (WPR/RC56.R8; [http://www2.wpro.who.int/rcm/en/archives/rc56/rc\\_resolutions/wpr\\_rc56\\_r08.htm](http://www2.wpro.who.int/rcm/en/archives/rc56/rc_resolutions/wpr_rc56_r08.htm)).

7 *Guidelines for certification of achievement of hepatitis B control goal in the Western Pacific Region*. Manila: World Health Organization Regional Office for the Western Pacific; 2007 ([www.wpro.who.int/entity/immunization/documents/docs/HepBControlCertifGuidelines.pdf](http://www.wpro.who.int/entity/immunization/documents/docs/HepBControlCertifGuidelines.pdf)).

8 Hepatitis B vaccines: WHO position paper. *Wkly Epidemiol Rec*. 2009;84(40):405–19.

9 Vaccinating health-care workers against hepatitis B. Manila: World Health Organization Regional Office for the Western Pacific; 2012 ([www.wpro.who.int/entity/immunization/documents/vaccinating\\_healthcare\\_workers\\_against\\_HepB\\_07092012.pdf](http://www.wpro.who.int/entity/immunization/documents/vaccinating_healthcare_workers_against_HepB_07092012.pdf)).

22nd meeting in June 2013, the WHO Regional Committee for the Western Pacific at its sixty-fourth session in October 2013, and the Second Hepatitis B Expert Resource Panel Consultation held in December 2013.

The guide is intended to provide a handy compilation of available guidance for hepatitis B vaccination programmes in countries and areas of the Western Pacific Region. It provides an update on the progress made since 2007, regional goals, programmatic strategies and indicators, processes for monitoring and verifying achievement of the hepatitis B control goal, and references to additional WHO resources.

## 1.2 CONTROL STRATEGIES

Universal infant immunization with three doses of hepatitis B vaccine, with the first dose provided within 24 hours of birth, is the most cost-effective prevention and control strategy. This strategy provides the earliest possible protection to future birth cohorts and reduces the pool of chronic carriers in the population. Timely vaccination of newborn infants (ideally within 24 hours of birth) can prevent perinatal transmission of hepatitis B. Catch-up vaccination of children born before the introduction of vaccine and vaccination of adults at high risk for HBV infection are additional preventive strategies that can help to protect older susceptible birth cohorts.

Non-immunization control options include ensuring the safety of blood and blood products through regular screening of donors, promotion of safe sex, and ensuring injection safety. These control strategies will have positive public health benefits, not only in terms of hepatitis B control, but also for other bloodborne infections, such as HIV. WHO has developed a comprehensive framework for global action on the prevention and control of viral hepatitis, which provides further guidance on non-vaccination control strategies for viral hepatitis including diagnosis and treatment.<sup>10</sup>

Notwithstanding the merits of these additional strategies, however, this updated reference guide focuses specifically on hepatitis B control through immunization.

**Universal infant immunization with three doses of hepatitis B vaccine, with the first dose provided within 24 hours of birth, is the most cost-effective prevention and control strategy.**

## 1.3 PROGRESS MADE IN THE WESTERN PACIFIC REGION

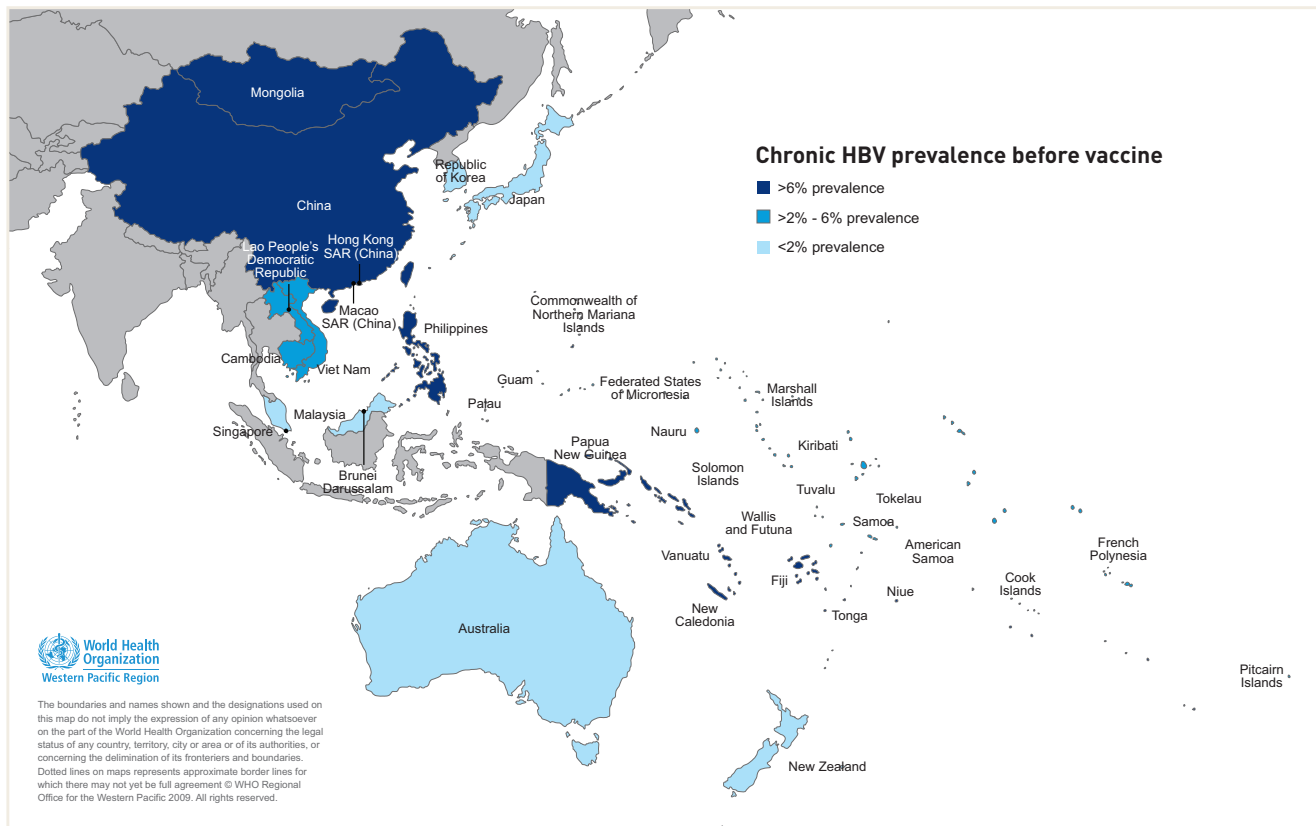
Since the publication of the 2007 hepatitis B regional plan, substantial progress in hepatitis B control has been made in the Region, including the achievement of the 2012 milestone of reducing chronic infection prevalence among 5-year-old children to less than 2%. Since 2005, all Member States in the Region, except Japan,<sup>11</sup> have been providing hepatitis B immunization for all infants nationwide. Since 2007, all Member States, except Japan and New Zealand,<sup>12</sup> have included a birth dose within 24 hours in their official immunization schedules. Reported coverage for hepatitis B birth dose and third dose has improved dramatically in the Region, although data quality remains a concern. The dramatic impact that vaccination programmes have had on reducing chronic infection prevalence in the Region is illustrated in Figures 1 and 2, and regional trends in vaccination coverage can be seen in Figure 3.

<sup>10</sup> Prevention and control of viral hepatitis infection: framework for global action. Geneva: World Health Organization; 2012 (WHO/HSE/PED/HIP/GHP 2012.1; [www.who.int/csr/disease/hepatitis/Framework/en/](http://www.who.int/csr/disease/hepatitis/Framework/en/)).

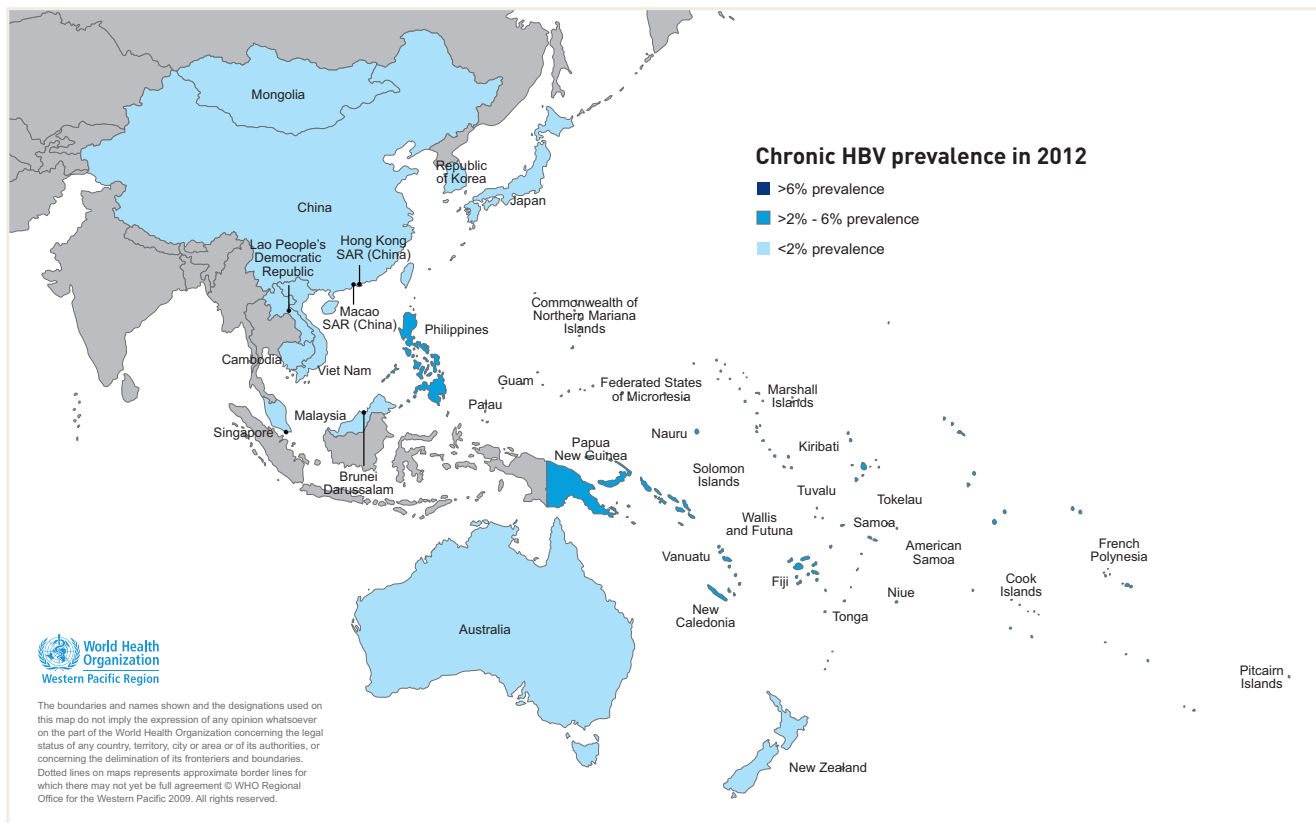
<sup>11</sup> Japan has a policy of screening all pregnant women and providing hepatitis B vaccination to infants born to HBsAg-positive mothers.

<sup>12</sup> Japan and New Zealand provide the birth dose to newborn infants born to HBsAg-positive women.

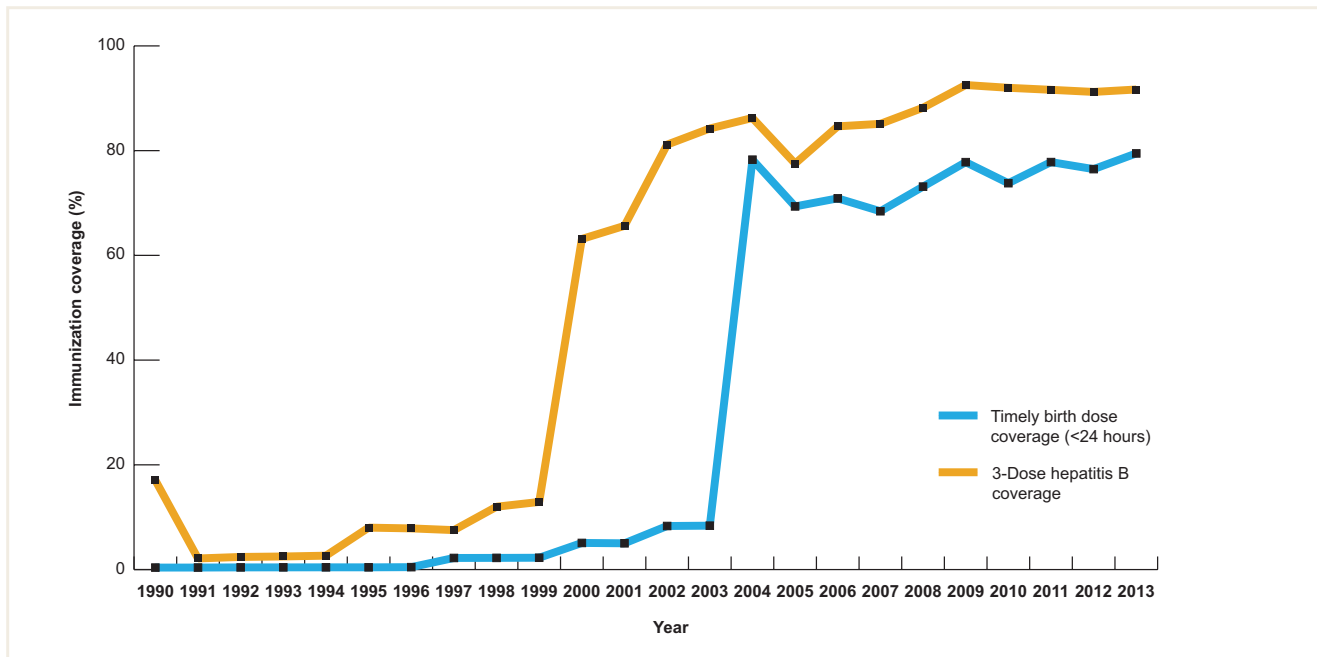
**Figure 1. Prevalence of chronic HBV among children before vaccine introduction**



**Figure 2. Prevalence of chronic HBV among children in 2012**

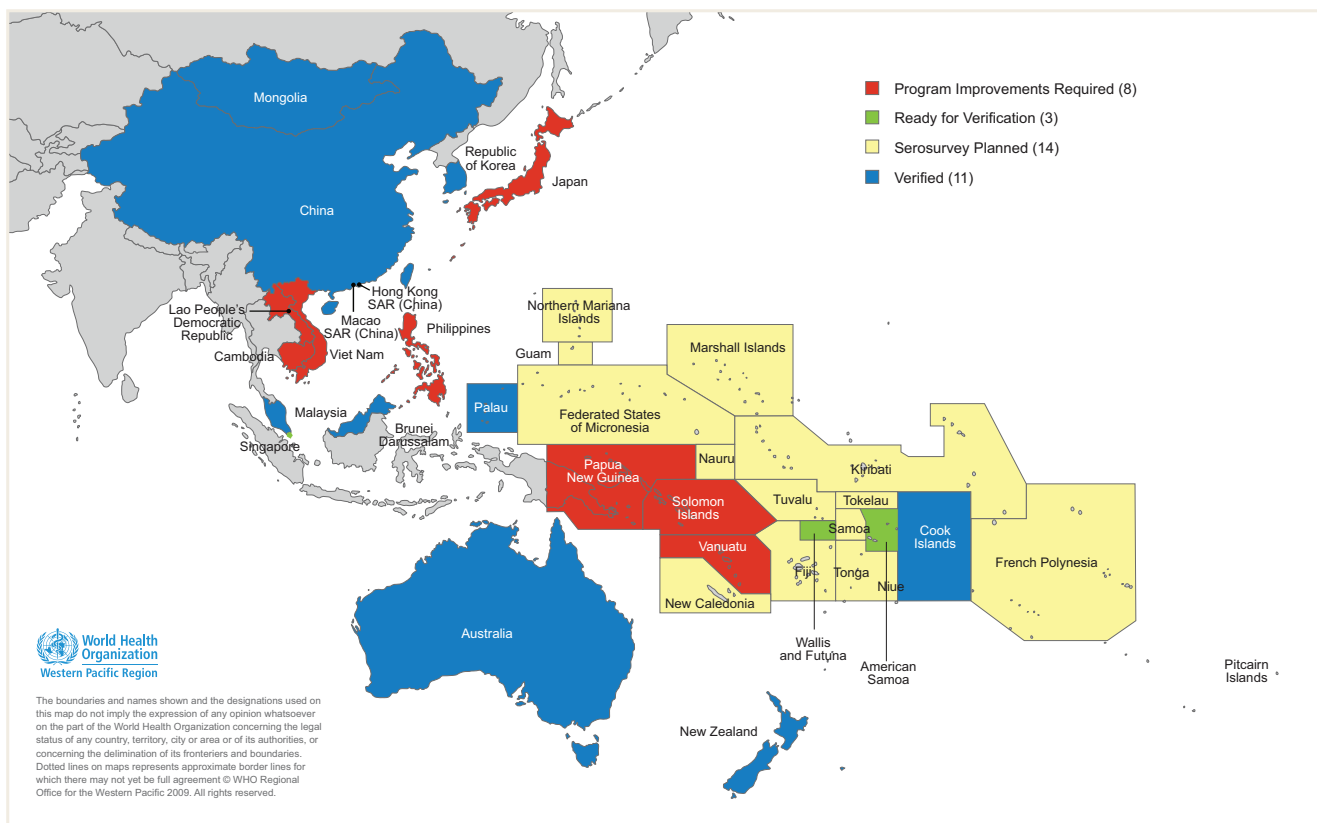


**Figure 3. Immunization coverage with hepatitis B birth dose and third dose, Western Pacific Region, 1990–2013**



As of 2012, the Region as a whole and at least 30 countries and areas have successfully reduced chronic infection rates in children to less than 2%. As of January 2014, 11 countries and areas were officially verified as achieving the goal of reducing infection rates in children to less than 1%: Australia, Brunei Darussalam, China, Hong Kong SAR (China), Cook Islands, Macao SAR (China), Malaysia, Mongolia, New Zealand, Palau and the Republic of Korea. See Figure 4.

**Figure 4. Hepatitis B control verification status, 2013**

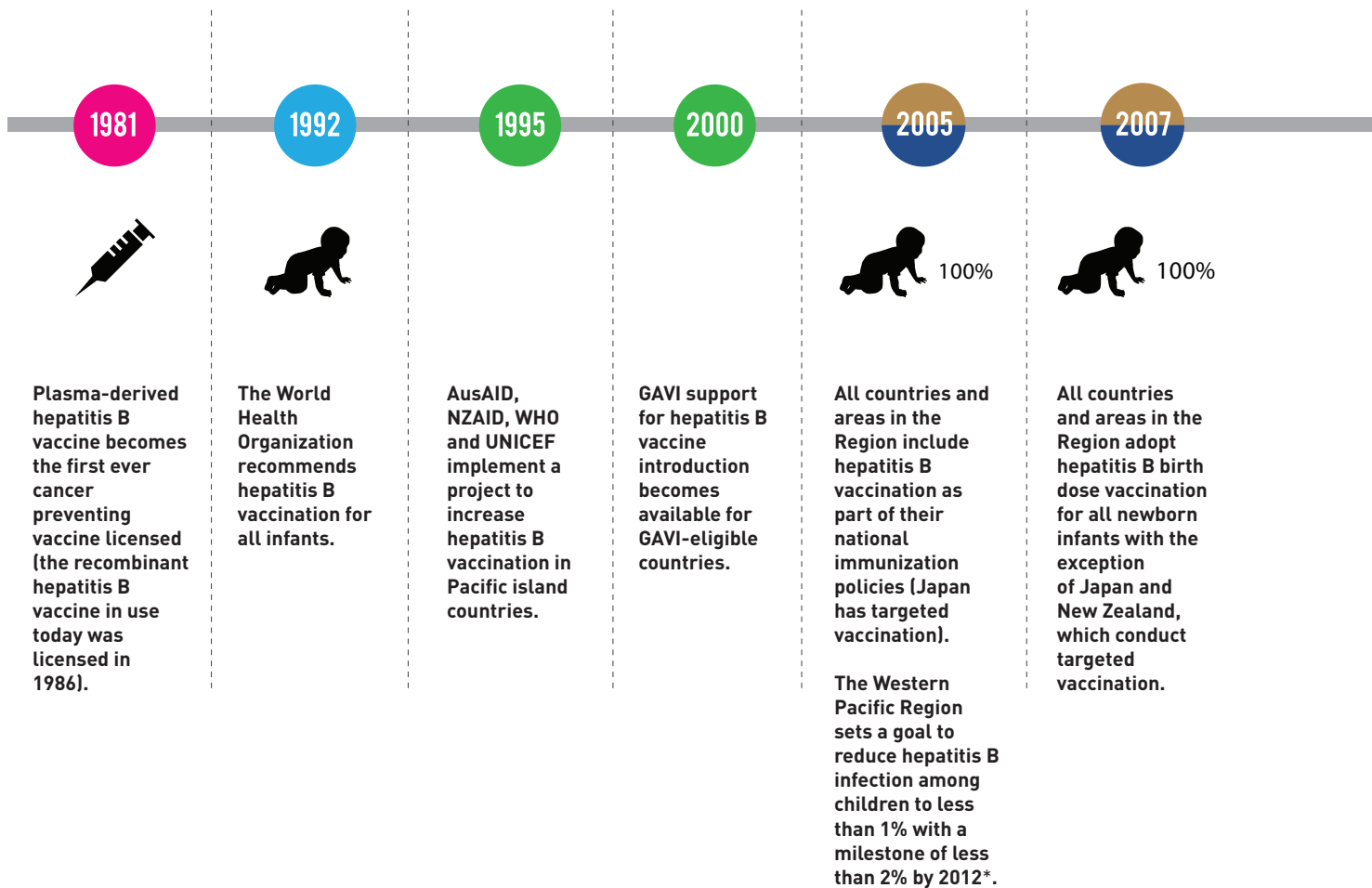


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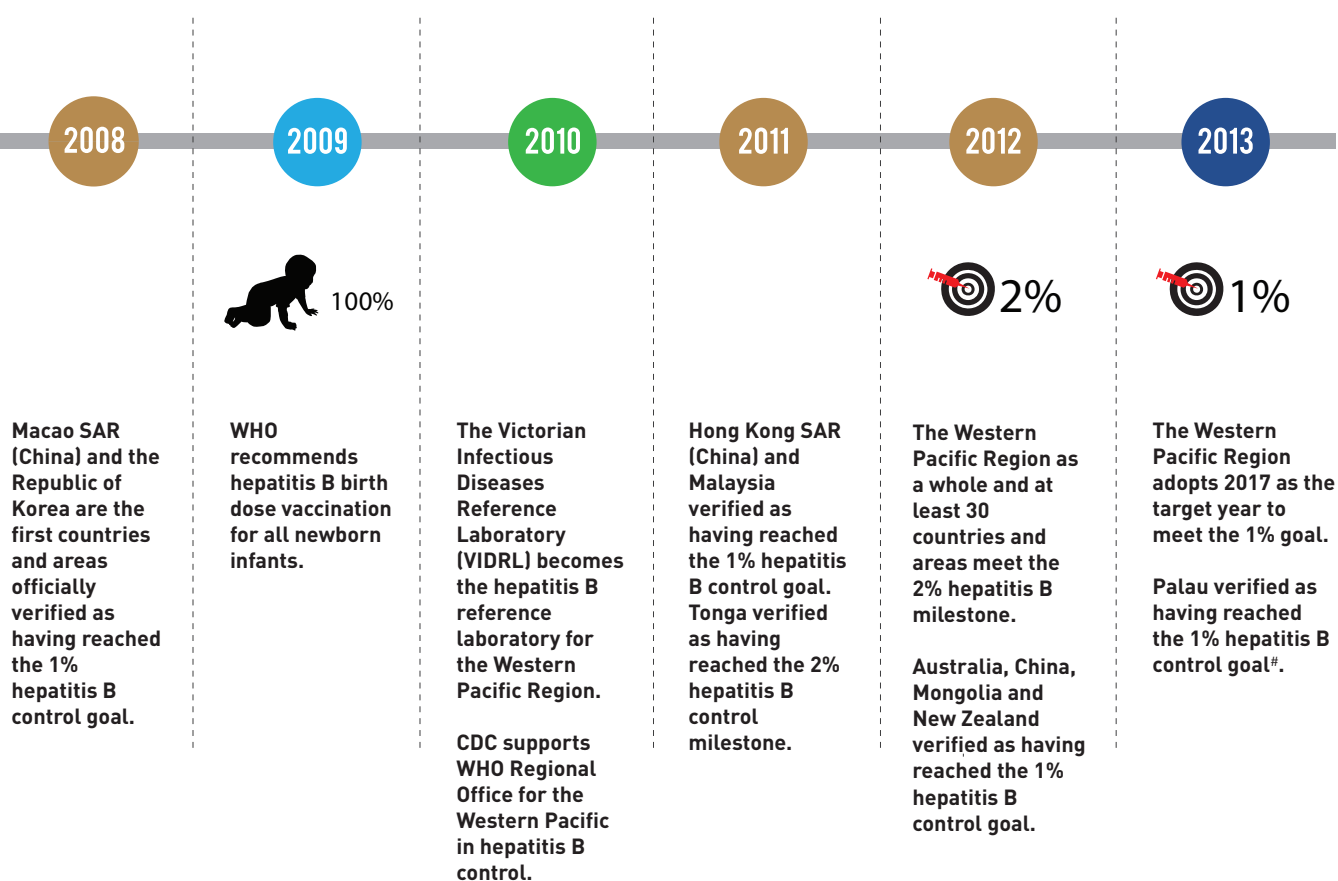
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## Key Milestones

Hepatitis B (HB)







\* WPR/RC56.8  
 # WPR/RC64.R5

### Further information

- More information on HBV, the consequences of HBV infection, and HBV epidemiology can be found in Annex 1.
- Additional information on hepatitis B vaccine can be found in Annex 2, and in the following resources:
  - WHO position paper on hepatitis B vaccines (2009): <http://www.who.int/wer/2009/wer8440.pdf>
  - Introducing hepatitis B vaccine into national immunization services (WHO/V&B/01/28): [http://whqlibdoc.who.int/hq/2001/WHO\\_V&B\\_01.28.pdf](http://whqlibdoc.who.int/hq/2001/WHO_V&B_01.28.pdf)
  - Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents (WHO/V&B/01.31): [http://whqlibdoc.who.int/hq/2001/WHO\\_V&B\\_01.31.pdf](http://whqlibdoc.who.int/hq/2001/WHO_V&B_01.31.pdf)
  - The Immunological Basis for Immunization Series: Hepatitis B (2012): [http://apps.who.int/iris/bitstream/10665/77755/1/9789241504751\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/77755/1/9789241504751_eng.pdf)
- Hepatitis B data profiles for the countries and areas of the Western Pacific Region, including demographic data, vaccination policies, childbirth delivery types, reported vaccination coverage during 2008–2012, and vaccination coverage and seroprevalence survey summaries, can be found in the following document:
  - Hepatitis B control: strategic information and country profiles. Manila: World Health Organization; 2013 (<http://www.wpro.who.int/hepatitis/resource/hepbcountryprofile.pdf>).



## 2. REGIONAL GOAL AND STRATEGIC AREAS OF FOCUS



## 2.1 REGIONAL HEPATITIS B CONTROL GOAL

**GOAL: Reduce HBsAg seroprevalence to less than 1% in 5-year-old children by 2017.**

The ultimate goal of the WHO Regional Office for the Western Pacific's Hepatitis B Programme is to protect each and every child from HBV infection. In September 2005, the Region pledged a commitment to reducing chronic HBV infection rates (as measured by HBsAg seroprevalence among children aged 5 years) to less than 2% by 2012.<sup>13</sup>

Having achieved that milestone in 2012, the sixty-fourth Regional Committee in 2013 resolved to meet the goal of reducing HBV infection in children to less than 1% prevalence by 2017 as measured by serological surveys (Boxes 1 and 2).<sup>14</sup>

Eleven countries and areas in the Western Pacific Region (Australia, Brunei Darussalam, China, Cook Islands, Hong Kong SAR [China], Macao SAR [China], Malaysia, Mongolia, New Zealand, Palau and the Republic of Korea) have already been verified as achieving the regional goal of less than 1% HBsAg seroprevalence. After verification, it is important to sustain high vaccination coverage, address pockets of low coverage, and strive to ensure that all new birth cohorts are completely protected from hepatitis B infection.

Eleven countries and areas in the Western Pacific Region have already been verified as achieving the regional goal of less than 1% HBsAg seroprevalence.

### Box 1: Why is hepatitis B infection measured in terms of HBsAg seroprevalence rather than clinical disease outcomes?

Vaccine-preventable diseases with strong active surveillance systems such as measles and polio:

- are acute in nature, meaning the impact of the vaccination programme is immediately visible in the same year on the disease burden in the targeted age group (for example, infants); and
- have distinct clinical signs and symptoms, which allow for the development of a simple case definition that can be used for detection of potential cases. This, coupled with laboratory confirmation, can achieve a highly sensitive surveillance system.

Neither of the above criteria applies to hepatitis B. Transmission of HBV among infants, the key target group for hepatitis B immunization programmes, is usually asymptomatic. Nevertheless, infants and younger children are highly prone to HBV infection from perinatal and horizontal transmission, and are more likely than adults to become chronically infected with HBV. These children are not only likely to die from cirrhosis or liver cancer in their 30s to 50s, but also serve as an infectious pool to sustain the transmission of HBV infection among the general population.

Therefore, surveillance for symptomatic hepatitis B disease among children (as practised for other vaccine-preventable diseases) is unlikely to show any impact of the vaccination programme.

The first indicator to be affected by a vaccination programme is the seroprevalence of HBsAg among the vaccinated cohorts, as fewer children become infected. Therefore, a reduction in chronic HBV infection can be verified by a decrease in the seroprevalence of serological markers (HBsAg) rather than a reduction in the incidence of cirrhosis or hepatocellular carcinoma, which would take several decades to observe.

13 Measles elimination, hepatitis B control and poliomyelitis eradication. Manila: World Health Organization Regional Office for the Western Pacific; 2005 (WPR/RC56.R8; [http://www2.wpro.who.int/rcm/en/archives/rc56/rc\\_resolutions/wpr\\_rc56\\_r08.htm](http://www2.wpro.who.int/rcm/en/archives/rc56/rc_resolutions/wpr_rc56_r08.htm)).

14 Hepatitis B control through vaccination: setting the target. Manila: World Health Organization Regional Office for the Western Pacific; 2013 (WPR/RC64.R5)

**Box 2: Why is the goal set among 5-year-old children?**

Children have a 90% chance of developing chronic HBV infection if infected at birth, a 30% chance if infected between the ages of 1 and 5 years, and only a 5–10% chance if infected after 5 years of age. In settings that are hyperendemic for hepatitis B, as is the case in most countries of the Western Pacific Region, most chronic infections are acquired by age 5.<sup>15</sup> As such, measuring the goal among children aged 5 years or older will take into account the complete exposure period when the risk of horizontal transmission and likelihood of becoming chronically infected are highest. Setting the goal among children under 5 years of age may overestimate the impact of vaccination programmes if some of the children who are uninfected and unprotected at the time of evaluation later become infected by age 5.

## 2.2 STRATEGIC AREAS OF FOCUS

The key strategic areas for hepatitis B prevention through vaccination are as follows:

- vaccination of infants;
- vaccination of priority adult population groups;
- vaccine supply and quality;
- advocacy and social mobilization; and
- measurement of programme performance and impact.

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15 Goldstein ST, Zhou F, Hadler S, Bell BP, Mast EE, Margolis HS. A mathematical model to estimate global hepatitis B disease burden and vaccination impact. *Int J Epidemiol*, 2005, 34:1329–39.

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### 3. VACCINATION OF INFANTS



Strengthening routine immunization services to achieve and sustain high coverage of each birth cohort with at least three doses of hepatitis B vaccine before the age of 1 year is the most important strategy for hepatitis B control. Mathematical modelling suggests that extremely high vaccination coverage is needed to interrupt hepatitis B transmission.<sup>16</sup> While it is difficult to know the exact coverage that is necessary to interrupt transmission of hepatitis B, the goal should be to protect the entire birth cohort to ensure equity in health access. When the Regional Committee set 2017 as the target year for achieving the goal of 1% hepatitis B prevalence, vaccination coverage targets were also endorsed. Based on the 2013 hepatitis B resolution, and the *Regional Framework for Implementation of the Global Vaccine Action Plan*, the coverage targets for both hepatitis B third dose and timely birth dose are at least 95% coverage at the national level, and at least 85% coverage in all districts.<sup>17</sup>

**Target: Minimum third dose coverage of 95% at the national level and at least 85% coverage in each district.**

The three-dose schedule for hepatitis B vaccine is combined with the schedules of DPT and *Haemophilus influenzae* type B (Hib) vaccine in the majority of countries of the Region. Monitoring hepatitis B third dose coverage is therefore an indicator of the overall strength of the routine immunization system in countries (Table 1).

**Target: Minimum birth dose coverage of 95% at the national level and 85% coverage at the district level.**

**Delivery of a timely birth dose (within 24 hours of birth) is critical to prevent mother-to-child transmission of HBV.**

Delivery of a timely birth dose (within 24 hours of birth) is critical to prevent mother-to-child transmission of HBV, a high priority in a region where women of childbearing age have chronic infection prevalence greater than 8% and prevalence of hepatitis B 'e' antigen (HBeAg) is high among those who are HBsAg positive.<sup>18</sup> A high percentage of chronic infections in the Region may be acquired through mother-to-child transmission during childbirth. The baby of an HBsAg-positive (carrier) mother has a 70–90% risk of infection if the mother is HBeAg positive, and a 5–20% (~10%) risk if she is HBeAg negative. Post-exposure prophylaxis with hepatitis B vaccine within 24 hours of birth dramatically reduces the risk of infection. A meta-analysis of randomized control trials found that birth dose vaccination reduced the incidence of hepatitis B chronic infection by 72% among infants born to HBsAg positive women.<sup>19</sup>

16 Goldstein ST, Zhou F, Hadler SC, Bell BP, Mast EE, Margolis HS. A mathematical model to estimate global hepatitis B disease burden and vaccination impact. *Int J Epidemiol.* 2005;34:1329–39.

17 Hepatitis B control through vaccination: setting the target. Manila: World Health Organization Regional Office for the Western Pacific; 2013 (WPR/RC64.R5, [http://www.wpro.who.int/about/regional\\_committee/64/resolutions/en/](http://www.wpro.who.int/about/regional_committee/64/resolutions/en/)).

18 Goldstein ST, Zhou F, Hadler SC, Bell BP, Mast EE, Margolis HS. A mathematical model to estimate global hepatitis B disease burden and vaccination impact. *Int J Epidemiol.* 2005;34:1329–39.

19 Lee C, Gong Y, Brok J, BOxall EH, Gluud C. Hepatitis B immunisation for newborn infants of hepatitis B surface antigen-positive mothers (Review). *The Cochrane Collaboration*; John Wiley & Sons, Ltd; 2008 ([http://www.who.int/immunization/sage/Lee\\_review\\_HepBinf\\_CD004790.pdf](http://www.who.int/immunization/sage/Lee_review_HepBinf_CD004790.pdf)).



Given the importance of early protection, timely delivery of the first dose of vaccine (within 24 hours of birth) for all newborn infants is the primary strategy for preventing perinatal transmission (Box 3). Where resources allow, hepatitis B immunoglobulin (HBIG) (passive immunity) may be given in addition to the vaccine to children born to HBsAg positive mothers. However, the option for HBIG is conditional on the existence of comprehensive antenatal screening programmes for hepatitis B infection and resources, and will be of limited value in settings with poor antenatal coverage. Where screening programmes exist, post-vaccination serological testing may be useful to assess the effectiveness of the programme in preventing mother-to-child infection. It is effective to conduct post-vaccination testing for HBsAg and anti HBs after completion of the vaccine series, between the ages of 9 and 18 months.

WHO in the Western Pacific Region has developed operational field guidelines for the delivery of the hepatitis B birth dose.<sup>20</sup> Countries may refer to this document when developing national action plans for delivery of the hepatitis B birth dose.

The birth dose should ideally be given within 24 hours of birth, as the earlier the vaccine is given the more likely it is that infection will be prevented. With limited data to establish when a birth dose is “too late” to protect the newborn infant, the birth dose should be administered on first possible postnatal contact, even if missed at birth. If the baby is due for the first combination dose (DTP-Hib-hepB) at the first contact, then the combination dose should be given rather than the monovalent birth dose.

### Box 3: Why is a birth dose for all newborn infants recommended?

WHO recommends a policy of universal neonatal vaccination within 24 hours of birth to ensure that all babies are provided initial protection at birth. Hepatitis B vaccination at birth provides benefits in terms of a “safety net”, not only for prevention of perinatal infection, but also against early horizontal transmission from household contacts or other sources.<sup>21</sup> In addition, administration of a birth dose has been associated with higher rates of on-time completion of the hepatitis B vaccine series and, in certain settings, improved completion rates for all other infant vaccines.

Antenatal screening programmes can be useful for identifying HBV infection among pregnant women. However, even where robust screening programmes are in place, country experiences have shown that targeted vaccination of babies of HBsAg positive mothers fails to capture all at-risk newborn babies due to incomplete screening, inaccurate test results, and errors in medical records. Therefore, universal birth dose vaccination is the most effective policy to prevent mother-to-child transmission.

Delivery of timely hepatitis B birth dose provides an opportunity to link immunization delivery systems with maternal health programmes (Box 6). It is effective for immunization services to work with maternal services work with maternal and neonatal care services to ensure that hepatitis B vaccine is included in the essential care package for newborn infants (Box 4), and to harmonize training and programmatic issues such as where, when, and by whom the birth dose will be given.

20 Preventing mother-to-child transmission of hepatitis B: Operational field guidelines for delivery of birth dose of hepatitis B vaccine. Manila: WHO Regional Office for the Western Pacific; 2006.

21 Schillie SF, Murphy TV. Seroprotection after recombinant hepatitis B vaccination among newborn infants: a review. *Vaccine*. 2013;31(21):2506–16.

**Box 4. Hepatitis B as part of the Essential Newborn Care package**

It is effective to include Hepatitis B vaccination in the essential newborn care package, so that it is part of the series of standard procedures that a baby receives at birth:

- Hepatitis B birth dose should be given after immediate newborn care (that is, drying baby, checking for breathing, skin-to-skin contact with mother, cord-cutting, initiation of breastfeeding, eye care) and only when the baby is stable (that is, baby scores 6 or higher on the Apgar test (if test is done) and is able to breastfeed soon after birth).
- Medications for the mother and baby should never be kept on the same tray to avoid programmatic errors.
- Hepatitis B birth dose can be administered along with other essential newborn care interventions such as BCG vaccination, vitamin K prophylaxis and weighing.
- Low birth weight and Caesarean sections are not contraindications for hepatitis B vaccination, although immunogenicity can be lower for low-birth-weight babies and for babies weighing less than 2,000 grams the birth dose and three additional doses are needed to provide complete protection.

Provision of the hepatitis B birth dose within 24 hours of birth provides special challenges, especially in countries where a substantial proportion of births occur at home. In many cases, home deliveries are handled by traditional birth attendants, most of whom receive no formal training. Collaboration with maternal and child health programmes to promote facility births and access to skilled birth attendants and postnatal care is of utmost importance, as well as engagement of village health volunteers and community leaders to increase access to outreach services available.

Ensuring population confidence in the safety of the vaccine is critical to achieving high vaccination coverage. Apprehensions about the timing and safety of administering vaccine immediately after birth, such as concerns about false contraindications and potential adverse reactions, must be addressed through education and training of health workers, as well as through information and communication aimed at the community, to avoid missed opportunities to vaccinate.

Low birth weight and premature delivery are NOT contraindications for the administration of hepatitis B vaccine within 24 hours of birth (Box 5). However, the birth dose should not interfere with any urgent clinical care needs that may present, and should only be given after the baby is stable. Studies have shown that the immunogenic response to the birth dose may be reduced in low-birth-weight babies. This should NOT prevent the administration of vaccine within 24 hours; however, it is crucial to ensure that low-birth-weight babies receive a full three-dose series of hepatitis B vaccine, *in addition* to the birth dose (a total of four doses).

The early postnatal period is a fragile time, and, in many developing countries, neonatal mortality remains high for various reasons. Over half of neonatal deaths occur within the first 24 hours of life,<sup>22</sup> increasing the likelihood of a coincidental association between birth dose vaccination and neonatal complications or death due to other causes. It is effective to train health-care providers to be able to answer questions about vaccine safety and address concerns about coincidental adverse events following immunization (AEFIs).

22 Newborn death and illness. Geneva: The Partnership for Maternal, Newborn & Child Health, World Health Organization; 2011 ([http://www.who.int/pmnch/media/press\\_materials/fs/fs\\_newborndeath\\_illness/en/index.html](http://www.who.int/pmnch/media/press_materials/fs/fs_newborndeath_illness/en/index.html), accessed in September 2014).

### Box 5. Contraindications and precautions

Extensive evidence has documented that the hepatitis B vaccine is extremely safe for neonates and infants.<sup>23,24</sup> Given the inherent fragility of the early neonatal period, however, health workers often hold misconceptions regarding contraindications for hepatitis B birth dose vaccination. It is therefore critical to improve education and training for health-care workers so that opportunities for immunization are not missed due to misinformation.

There are no absolute contraindications for timely hepatitis B birth dose vaccination.

**Low birth weight, premature delivery, Caesarean sections and HIV status are NOT contraindications for the administration of the vaccine.** However, the timing of vaccine administration should not interfere with treatment of any urgent neonatal care, and should be given only after the baby is stable.

**Table 1. Typical schedule of hepatitis B (HepB) and pentavalent (DTP-Hib-hepB) vaccination in the Western Pacific Region\***

Age**	Vaccine
At birth (within 24 hours)	HepB monovalent
6 weeks	DTP–HepB–Hib1
10 weeks	DTP–HepB–Hib2
14 weeks	DTP–HepB–Hib3

\* While three doses are sufficient to induce immunity, for programmatic reasons most countries in the Region use a combination vaccine, resulting in a four-dose schedule.

\*\* Ages given are recommended as the earliest possible, but they are flexible. Immunization programmes should emphasize vaccination at birth and completing the hepatitis B series by 6 months of age.

### Catch-up immunization of older children

The first priority is protecting infants through strengthening routine immunization services. Catch-up immunization for older children who missed immunization as infants is recommended as a secondary strategy after routine infant vaccination reaches target levels if countries have additional financial and human resources for enhanced hepatitis B control, and should be based on careful epidemiological and economic analysis. It is up to each country to prioritize other groups for publicly funded immunization.

### Effective Strategies:

1. Use tools, such as the Reaching Every District (RED) strategy (re-establishing outreach services, supportive supervision at all levels, linking services with communities, monitoring and use of data for action, and planning and management of resources) to streamline and strengthen routine immunization services to reach each and every child. For more information on tools and guidance for immunization service delivery, including the RED strategy, visit WHO’s Service Delivery webpage.<sup>25</sup>
2. Collaborate with maternal and child health programmes to coordinate immunization services with broader maternal and neonatal care; improve policies, training and supervision; increase

23 Lewis E, Shinefield HR, Woodruff BA, Black SB, Destefano F, Chen RT, et al. Safety of neonatal hepatitis B vaccine administration. *Pediatr Infect Dis J*. 2001;20(11):1049–54.

24 Eriksen EM, Perlman JA, Miller A, Marcy SM, Lee H, Vadheim C, et al. Lack of association between hepatitis B birth immunization and neonatal death: a population-based study from the vaccine safety datalink project. *Pediatr Infect Dis J*. 2004;23(7):656–61.

25 Immunization, vaccines and biological: service delivery (webpage). Geneva: World Health Organization; 2014 ([http://www.who.int/immunization/programmes\\_systems/service\\_delivery/en/](http://www.who.int/immunization/programmes_systems/service_delivery/en/))

- access to delivery by a skilled birth attendant; and ensure safe provision of birth dose within 24 hours for all institutional and home births. For more information on effective strategies for improving coverage, refer to WHO's *Practices to improve coverage of the hepatitis B birth dose vaccine*,<sup>26</sup> and *Consultation on Improving and Monitoring Hepatitis B Birth Dose Vaccination*.<sup>27</sup>
3. Ensure availability of vaccine, hepatitis B policy and standing orders (required procedures) for administration of birth dose in the delivery room or postnatal ward for all newborn infants, including those born via Caesarean section. Ensure that these are disseminated to private facilities as well as government facilities (Box 8).
  4. Focus particular efforts on poor-performing districts and high-prevalence groups, identified through improved data collection, mapping and regular analysis of subnational/district-level coverage data. See Chapter 7 for more on monitoring district-level coverage.
  5. For countries with low birth dose coverage, consider conducting an assessment of birth dose practices to identify main barriers to birth dose vaccination. Such assessments have been conducted in Cambodia, the Lao People's Democratic Republic and the Philippines.<sup>28</sup>
  6. Promote the use of controlled temperature chain (CTC) for hepatitis B vaccine to increase coverage with the birth dose in health facilities with no continuous cold chain and for home births. See Box 7 for more information on CTC, and refer to Western Pacific Regional Office's operational field guidelines for detailed instructions on out-of-cold-chain use of hepatitis B vaccine.<sup>29</sup>
  7. Increase health promotion efforts and communication aimed at parents to increase demand for hepatitis vaccination.

#### Box 6. Success from the field: China

China has made remarkable progress in increasing immunization coverage of hepatitis B vaccine, through large-scale rollouts of birth dose vaccination, followed by a major catch-up campaign in 2009. Demonstration projects (which ran from 2005 to 2009) focused on promoting hospital delivery, strengthening collaboration between the Expanded Programme Immunization (EPI) and the maternal and child health programme, and developing strategies for both hospital and home births, and resulted in marked increases in timely birth dose coverage for both facility- and home-delivered babies.

Strategies for promoting hospital delivery included development of a rural health insurance scheme and reimbursement of expenses for hospital delivery. These projects contributed not only to the improvement of hepatitis birth dose coverage, but also to a reduction in overall maternal mortality and acceleration of neonatal tetanus elimination.

Collaboration with maternal and child health teams helped enforce the policy of registering target infants into the EPI system before their birth to avoid any missed opportunities for vaccination.

Strategies to improve coverage for hospital births included ensuring availability of vaccine, re-training health workers, and designating one focal staff responsible through the entire process of delivery assistance to administration and recording of birth dose vaccination. Strategies aimed at home deliveries involved enhancing education for parents and village birth attendants, encouraging registration of pregnant women, and ensuring subsidies for village doctors to administer timely birth dose.

26 *Practices to improve coverage of the hepatitis B birth dose vaccine*. Geneva: World Health Organization; 2012 (WHO/IVB/12.11; [http://www.who.int/immunization/documents/control/who\\_ivb\\_12.11/en/](http://www.who.int/immunization/documents/control/who_ivb_12.11/en/)).

27 *Consultation on Improving and Monitoring Hepatitis B Birth Dose Vaccination*. Manila: World Health Organization Regional Office for the Western Pacific; 2012 (WPR/DCC/EPI(03)/2012; [http://www.wpro.who.int/immunization/documents/consultation\\_HepB\\_birthdose\\_June2012\\_mtgrpt.pdf](http://www.wpro.who.int/immunization/documents/consultation_HepB_birthdose_June2012_mtgrpt.pdf)).

28 Patel MK, Capeding RZ, Ducusin JU, de Quiroz Castro M, Garcia LC, Hennessey K. Findings from a hepatitis B birth dose assessment in health facilities in the Philippines: Opportunities to engage the private sector. *Vaccine*. 2013 (in press).

29 *Preventing mother-to-child transmission of hepatitis B: Operational field guidelines for delivery of birth dose of hepatitis B vaccine*. Manila: WHO Regional Office for the Western Pacific; 2006.

**Box 7. Controlled temperature chain (CTC)**

As hepatitis B vaccine is relatively heat-stable and retains its potency even after storage out of the cold chain, CTC can be especially useful for the timely provision of the birth dose for babies born either at home or in health centres that lack cold chain capacity. Vaccine vial monitors (VVM) are used to ensure that cumulative heat exposure does not exceed the limit for that vaccine. VVM30, the most thermo-stable variety of four types of VVM, is currently recommended for the hepatitis B vaccine, and provides the opportunity to use these vaccines after exposure to ambient temperature for up to one month. In addition, the availability of monovalent hepatitis B vaccine in prefilled, single-dose injection devices (e.g. Uniject™) can facilitate the administration of the vaccine by birth attendants to infants delivered at home.<sup>30</sup>

**Recommended indicators:**

- (1) Percentage of infants vaccinated with three doses of vaccine by age 1 year at national level and at each subnational/district level.
- (2) Percentage of districts with greater than 85% coverage with three doses of vaccine.
- (3) Percentage of newborn infants given timely birth dose (within 24 hours of birth) at national level and at each subnational/district level. If possible, it is helpful to monitor birth dose coverage separately for health-facility births and home births.
- (4) Percentage of newborn infants given any birth dose (>24 hours, up until the time of the first combination dose), at national level and at each subnational/district level. If possible, it is helpful to monitor birth dose coverage separately for health-facility births and home births.
- (5) Percentage of districts with greater than 85% timely hepatitis B birth dose coverage.
- (6) Existence and implementation of birth dose vaccination operational plans.
- (7) Programme monitoring: implementation of training, supervision, outreach services, and integration with other maternal and child health programmes.

**As hepatitis B vaccine is relatively heat-stable and retains its potency even after storage out of the cold chain, CTC can be especially useful for the timely provision of the birth dose for babies born either at home or in health centres that lack cold chain capacity.**

30 Sutanto A, Suarnawa IM, Nelson CM, Stewart T, Soewarso TI. Home delivery of heat-stable hepatitis B vaccines in Indonesia: outreach immunization with a prefilled, single-use injection device. *Bull World Health Organ.* 1999;77:119–26.

**Box 8: Effective practices for improving hepatitis B birth dose coverage****Service delivery arrangements**

- Encourage health-facility deliveries through subsidized deliveries, provide education to mothers during antenatal care and enhance links with communities.
- Issue standing orders for birth dose vaccination in all health facilities.
- Orient health and administrative staff on the HBV policy.
- Integrate birth dose with maternal and newborn care in health facilities by:
  - ensuring vaccine is available in the delivery room or postnatal ward;
  - establishing clear health-facility policies on where/when/who is to vaccinate;
  - positioning birth dose vaccination as part of essential newborn care package; and
  - providing supportive supervision.
- Ensure private facilities provide birth dose vaccination.
- Where infants are born outside health facilities:
  - conduct home visits to provide timely vaccination;
  - integrate timely birth dose with home visits for other early postnatal care;
  - store vaccine outside the standard cold chain in CTC; and
  - engage village health volunteers to inform health facility of all home births.

**Health workforce considerations**

- Conduct well-structured training for health workers, including education on perinatal transmission, backed up by frequent follow-up and supportive supervision.

**Health information system strengthening**

- Maintain birth registries and community birth notification, including tracking home births.
- Incorporate birth dose and its timing within vaccination records.
- Use accurate definition of timely birth dose in coverage reporting.

**Education**

- Address community concerns or lack of knowledge regarding birth dose.
- Address fear of adverse events, including planning for the risk of coincidental newborn death or disease.
- Respond to parental refusal of vaccination.

**Further information:**

- Consultation on Improving and Monitoring Hepatitis B Birth Dose Vaccination, Manila, Philippines, 13–15 June 2012 (WPR/DCC/EPI(03)/2012): [www.wpro.who.int/entity/immunization/documents/consultation\\_HepB\\_birthdose\\_June2012\\_mtgprpt.pdf](http://www.wpro.who.int/entity/immunization/documents/consultation_HepB_birthdose_June2012_mtgprpt.pdf)
- Practices to improve coverage of the hepatitis B birth dose vaccine (WHO/IVB/12.11): [http://apps.who.int/iris/bitstream/10665/78616/1/WHO\\_IVB\\_12.11\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/78616/1/WHO_IVB_12.11_eng.pdf)
- Preventing mother-to-child transmission of hepatitis B: Operational field guidelines for delivery of the birth dose of hepatitis B vaccine (2006): [www.wpro.who.int/immunization/documents/docs/HepBOperationalFieldGuidelines.pdf](http://www.wpro.who.int/immunization/documents/docs/HepBOperationalFieldGuidelines.pdf)



## **4. VACCINATION OF PRIORITY ADULT POPULATION GROUPS**

**Incidence of acute HBV infection is highest among adolescents and adults, although the risk of developing chronic HBV infection is low compared to infants and children.**

The immunization of high-risk adult population groups may be prioritized after infant immunization. Groups considered at high risk for HBV transmission include contacts of HBsAg-positive persons, health workers, men who have sex with men, sex workers, people who inject drugs, frequent recipients of blood or plasma transfusions, as well as any other groups coming in regular contact with blood and blood products.

Incidence of acute HBV infection is highest among adolescents and adults, although the risk of developing chronic HBV infection is low compared to infants and children. Vaccination programmes targeting high-risk adult groups can be difficult to implement, primarily because of problems in identifying and vaccinating persons engaged in high-risk activities before they become infected.<sup>31</sup> Health-care workers are often unaware of groups at high risk of acquiring HBV infection and may not identify such clients during routine health-care visits. Currently, there is only limited vaccination of susceptible household and sexual contacts of HBsAg-positive persons identified in screening programmes in most Member States in the Region.

**Universal vaccination of health-care workers is an effective strategy to protect high risk adult groups from hepatitis B infection**

Due to the nature of their work and frequent contact with blood products and potentially contaminated materials, health-care workers are at increased risk of exposure to HBV. Since health-care workers are a well-identified and accessible group to target for vaccination programmes, developing regulations to vaccinate health workers is an effective strategy to protect this high risk group.<sup>32</sup> The ideal policy is mandatory hepatitis B vaccination during training (that is, nursing school or medical school) so that health workers are protected before they encounter opportunities for infection. Hepatitis B vaccination can be combined with vaccination of health-care workers for measles and rubella. It is effective to monitor health worker vaccination policies monitored to ensure compliance (for example, all health workers should provide proof of vaccination as a job entry requirement).

A regional guidance document has been developed to encourage countries to establish programmes to routinely vaccinate the incoming health workforce, and offer vaccination opportunities to all current health workers.<sup>33</sup> The full course required is three doses: an initial dose; a second dose given one month after the initial dose; and a third dose given six months after the initial dose.

### **Effective Strategies:**

1. Increase awareness among health-care workers and the general public on the risk factors for hepatitis B infection and the importance of vaccination.
2. Advocate for a strong health-worker vaccination policy such as mandatory free vaccination as a legal requirement for job entry.

31 Centers for Disease Control and Prevention (CDC). Hepatitis B virus: A comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination: Recommendation of the Immunization Practices Advisory Committee (ACIP). *MMWR*. 1991;40(RR-13):1–19.

32 Global action plan on workers health 2008-2017 [http://apps.who.int/gb/ebwha/pdf\\_files/WHASSA\\_WHA60-Rec1/E/WHASS1\\_WHA60REC1-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHASSA_WHA60-Rec1/E/WHASS1_WHA60REC1-en.pdf)

33 Vaccinating health-care workers against hepatitis B. Manila: World Health Organization Regional Office for the Western Pacific; 2012.



3. Offer vaccination to all existing health workers. Consider catch-up campaigns in areas where universal mandatory vaccination is still being rolled out.

**Recommended indicators:**

- (1) Existence of an official hepatitis B vaccination policy for all health workers
- (2) Percentage of clinical health workers who have received hepatitis B vaccine
- (3) Implementation of advocacy, training and supervision for health worker vaccination

**Further information:**

Vaccinating health-care workers against hepatitis B. WHO Western Pacific Region (2012):  
<http://www.wpro.who.int/immunization/documents/docs/HepBVaccinatingHCW.pdf>





## 5. VACCINE SUPPLY, QUALITY AND SAFETY



**Bottlenecks at any step in the supply chain may result in interrupted availability of vaccine, including political or financial constraints, poor forecasting and ordering processes, and poor vaccine distribution.**

The availability of an adequate supply of high-quality vaccines and safe injection equipment is critical to the success of every immunization service. Stock-outs of vaccine are still a problem in the Region, and these missed opportunities for vaccination have serious consequences for disease transmission.

Bottlenecks at any step in the supply chain may result in interrupted availability of vaccine, including political or financial constraints, poor forecasting and ordering processes, and poor vaccine distribution. Effective management and storage of vaccines can eliminate occurrences of vaccine stock-outs and considerably reduce vaccine wastage. WHO has developed tools and resources to help countries with appropriate vaccine forecasting and supply management.<sup>34</sup> In case of a shortage of monovalent vaccine, priority should be given to high-volume vaccination centres such as hospitals and birthing centres (See Box 9 to learn more about the impact of vaccine stock-outs in Cambodia).

Vaccine stock-outs can be avoided by adhering to strong stock management practices, including:

- appropriate vaccine-financing and demand-forecasting systems;
- standardized recording and reporting of all vaccine stock transactions;
- maintenance of buffer stock for vaccines and other consumables (allowing sufficient lead-time with new orders, to ensure uninterrupted supply);
- conduct of periodic physical inventories (at least once every three months); and
- establishment of good warehousing practices (ensuring stock security, data security, appropriate storage, cleanliness and supervision).

#### **Box 9. Impact of vaccine stock-outs**

In 2012, Cambodia experienced a stock-out of hepatitis B monovalent vaccine. During the four months that vaccine was not available, it was estimated that 3062 babies were infected with HBV. Half of these chronically infected babies would go on to develop liver problems, and one in four would eventually die of liver failure or liver cancer—an estimated 766 deaths that could have been avoided by ensuring continuous stock of birth dose vaccine.

Concerns about vaccine wastage should not interfere with the priority of universal birth dose coverage. For countries using multi-dose vials, there will inevitably be a certain amount of wastage, but this should not be a barrier to administering the vaccine. The WHO policy for use of opened, multi-dose vials<sup>35</sup> states that opened vials of hepatitis B vaccine may be used for up to one month, provided appropriate storage conditions are maintained, aseptic techniques for withdrawal are followed, and the expiry dates and VVMs have not passed the discard point. The opened, multi-dose vial policy cannot be used for vials kept out of the cold chain. For small facilities with few births per month or facilities using the vaccine out of the cold chain, single-dose vials can be procured to reduce vaccine wastage.

Hepatitis B vaccine is very freeze-sensitive (the freezing point is about -0.5 oC).<sup>36</sup> Freeze damage is the greatest threat to the vaccine's integrity, as freezing permanently destroys

34 Vaccine management and logistics – logistics support (webpage). Manila: World Health Organization Regional Office for the Western Pacific; 2013 [http://www.who.int/immunization/programmes\\_systems/supply\\_chain/resources/tools/en/](http://www.who.int/immunization/programmes_systems/supply_chain/resources/tools/en/)

35 WHO Policy Statement: The use of opened multi-dose vials of vaccine in subsequent immunization sessions. Geneva: World Health Organization; 2000 (WHO/V&B/00.09; [http://whqlibdoc.who.int/hq/2000/WHO\\_V&B\\_00.09.pdf](http://whqlibdoc.who.int/hq/2000/WHO_V&B_00.09.pdf))

36 Temperature sensitivity of vaccines. Geneva: World Health Organization; 2006 (WHO/IBV/06.10; [http://whqlibdoc.who.int/hq/2006/WHO\\_IVB\\_06.10\\_eng.pdf](http://whqlibdoc.who.int/hq/2006/WHO_IVB_06.10_eng.pdf))

potency, resulting in considerably reduced vaccine efficacy. To ensure optimal potency of all hepatitis B vaccines, countries must pay careful attention to handling practices, including the storage and transport of vaccine from the primary vaccine store to the end-user at the health facility, and further down to outreach sites.

Staff working at all levels should be trained regularly on correct vaccine-storage practices and the importance of preventing inadvertent freezing. Clear operational guidelines should be implemented, and all supervision visits should include temperature monitoring and checking for vaccine freezing.

Many temperature-monitoring studies have indicated that vaccines are more likely to be frozen during transportation than while in storage at a health facility. Special attention is needed to ensure that vaccine is not frozen while being transported, and the condition of the vaccines on arrival, including the state of freeze indicators, should be assessed and recorded for every shipment. Additional information on preventing freeze damage to vaccines, including best practices, is outlined in a WHO aide-memoire.<sup>37</sup>

Adherence to safe injection practices is an important aspect of all immunization programmes. Unsafe injections not only can result in injury and transmission of pathogens, but also can cause non-infectious adverse events such as abscesses and toxic reactions, all of which can seriously undermine public trust in vaccines. Proper vaccine safety training should include best practices on hygiene and sterile equipment, proper injection techniques, and safe disposal of sharps and other waste products.

**Unsafe injections not only can result in injury and transmission of pathogens, but also can cause non-infectious adverse events such as abscesses and toxic reactions, all of which can seriously undermine public trust in vaccines.**

### Effective Strategies:

1. Improve vaccine stock management to ensure uninterrupted supply of quality vaccine.
2. Ensure sustained financing and timely procurement of vaccine supply.
3. Reduce vaccine wastage by using smaller vial formulations for small health facilities.
4. Prevent inadvertent vaccine freezing through monitoring of freeze tags or other devices.
5. Improve training in cold chain management and promotion of use of CTC in appropriate contexts.

### Recommended indicators:

- (1) Number and length of vaccine stock-outs at the national provincial, and district levels.
- (2) Implementation of guidelines, training and supervision of vaccine management and safe injection practices.

### Further information:

- Vaccine management and logistics – Logistics support tools: [http://www.who.int/immunization/programmes\\_systems/supply\\_chain/resources/tools/en](http://www.who.int/immunization/programmes_systems/supply_chain/resources/tools/en)
- Training for mid-level managers (MLM), module 1: Cold chain, vaccines and safe-injection equipment management (WHO/IVB/08.01):[http://whqlibdoc.who.int/hq/2008/WHO\\_IVB\\_08.01\\_eng.pdf](http://whqlibdoc.who.int/hq/2008/WHO_IVB_08.01_eng.pdf)
- WHO Policy Statement: The use of opened multi-dose vials of vaccine in subsequent immunization sessions (WHO/V&B/00.09): [http://whqlibdoc.who.int/hq/2000/WHO\\_V&B\\_00.09.pdf](http://whqlibdoc.who.int/hq/2000/WHO_V&B_00.09.pdf)

37 Aide-memoire for prevention of freeze damage to vaccines. Geneva: World Health Organization; (WHO/IVB/07.09; [http://www.who.int/immunization/documents/WHO\\_IVB\\_07.09/en/](http://www.who.int/immunization/documents/WHO_IVB_07.09/en/)).

- Aide-memoire for prevention of freeze damage to vaccines (WHO/IVB/07.09): [http://whqlibdoc.who.int/hq/2007/WHO\\_IVB\\_07.09\\_eng.pdf](http://whqlibdoc.who.int/hq/2007/WHO_IVB_07.09_eng.pdf)
- Temperature sensitivity of vaccines (WHO/IBV/06.10): [http://whqlibdoc.who.int/hq/2006/WHO\\_IVB\\_06.10\\_eng.pdf](http://whqlibdoc.who.int/hq/2006/WHO_IVB_06.10_eng.pdf)
- WHO Western Pacific Region – Immunization Safety (website): [http://www.wpro.who.int/topics/immunization\\_safety/en](http://www.wpro.who.int/topics/immunization_safety/en)
- WHO best practices for injections and related procedures toolkit (WHO/EHT/10.02): [http://whqlibdoc.who.int/publications/2010/9789241599252\\_eng.pdf?ua=1](http://whqlibdoc.who.int/publications/2010/9789241599252_eng.pdf?ua=1)



**INFORMED?**

## 6. ADVOCACY AND SOCIAL MOBILIZATION

**UNAWARE?**

VIRAL HEPATITIS KILLS  
1.5 MILLION PEOPLE WORLDWIDE  
EACH YEAR.  
THAT'S AS MANY PEOPLE  
AS HIV / AIDS.

HEPATITIS: THINK AGAIN  
**#thinkhepatitis**

World Hepatitis  
Alliance

Think hepatitis

**Perceptions and attitudes of health staff are important determinants of willingness to vaccinate newborn infants.**

Despite progress made in the Western Pacific Region in recent years, there remains a considerable lack of awareness, in the public and among some health providers and decision-makers, of the risks and consequences of hepatitis B infection and of the importance of vaccination. Advocacy, communication and social mobilization are important for immunization programmes in general, but are especially critical for hepatitis B because:

- HBV infections are largely silent (that is, no external manifestation) among infants and children;
- onset of clinical manifestation of chronic HBV infection is very delayed;
- the link between hepatitis B infection in early childhood and liver disease (for example, cirrhosis or hepatic cellular carcinoma) is not well understood; and
- directly recognizable deaths (for example, from fulminant hepatitis B) are few.

As a result, the benefits of childhood hepatitis B vaccination have a delayed visible impact on morbidity and mortality, and thus are not immediately appreciated.

Advocacy targets leaders and decision-makers to engender political commitment, advance policy creation and ensure availability of sufficient resources for programme implementation. Advocacy is important for raising awareness of HBV as a cause of disease and death, as well as for the benefits of hepatitis B immunization and importance of timely birth dose delivery. Political commitment, as well as support from trusted voices of the health service sector and community influencers, is necessary to provide credible and consistent messages on the benefits of vaccination.

Perceptions and attitudes of health staff are important determinants of willingness to vaccinate newborn infants. Monitoring and improving the knowledge of health workers is key to improving the coverage and quality of immunization services.

Social mobilization, focused on increasing awareness within communities, is important to create demand for and improve uptake of hepatitis B immunization services. Fear of adverse events or harm, in particular, has been documented as a barrier to birth dose vaccination.<sup>38</sup> The possibility of coincidental newborn death, in addition to broader community concerns that may be raised against vaccination in general, emphasizes the need for hepatitis B immunization programmes to prepare communications for a pre-emptive response to adverse perceptions (see Box 10 for lessons from Viet Nam).

Given the devastating effects that misinterpretation and miscommunication of vaccine safety issues can have on vaccination programmes, it is crucial to develop strong training and communication materials that are readily available in order to maintain public trust in vaccines. Collaboration with the media is important to ensure access to current and credible sources for the dissemination of accurate and evidence-based key messages. Regular workshops are also a useful way to inform and sensitize the media to issues around immunization and AEFIs, so that information is conveyed to the public accurately and objectively. A useful resource on vaccine safety communication has been developed by the WHO Regional Office for the Western Pacific.<sup>39</sup>

38 Practices to improve coverage of the hepatitis B birth dose vaccine Geneva: World Health Organization; 2012 (WHO/IVB/12.11; [http://www.who.int/immunization/documents/control/who\\_ivb\\_12.11/en/](http://www.who.int/immunization/documents/control/who_ivb_12.11/en/)).

39 Vaccine safety communication: Guidelines for immunization programme managers/National Regulatory Authority. Manila: World Health Organization Regional Office for the Western Pacific; 2014.



### Box 10. AEFI preparedness: Lessons from Viet Nam

Viet Nam's timely hepatitis B birth dose coverage reached 64% in 2006. However, after reports of adverse events following administration of the vaccine, coverage levels dropped to 29% in 2007, and 26% in 2008. An independent group investigated the AEFIs and concluded that there was no causal association between the deaths and the vaccine.<sup>40</sup> Additional AEFIs in 2012 and 2013 were highlighted in the media and have continued to adversely impact the hepatitis B vaccination coverage.

The situation in Viet Nam provides a valuable lesson about the impact that AEFIs can have on immunization programmes, and highlights the importance of prompt investigation and response, development of pre-emptive communication strategies that anticipate AEFIs, education of health workers to address concerns, and coordination of information with media.

A proactive approach with the media, for example, conducting technical briefings and media workshops, issuing regular press releases, and inviting senior public health officials to serve as spokespersons, can facilitate balanced coverage when AEFIs occur.

## Partners in Hepatitis B control

Partners have played an integral part in hepatitis B control in the Western Pacific Region. In many countries, the introduction of hepatitis B vaccine has relied heavily on the support of the governments of Australia and New Zealand, WHO, United Nations Children's Fund (UNICEF) and the Gavi, the Vaccine Alliance. Other key partners include the Burnet Institute of Australia, the governments of Japan and Luxembourg, PATH, Stanford University's Asian Liver Center, the United States Centers for Disease Control and Prevention (US CDC), and the ZeShan Foundation in Hong Kong SAR (China). In addition, the Victorian Infectious Diseases Reference Laboratory in Melbourne, Australia, was established as the Western Pacific Region's regional reference laboratory for hepatitis B in 2010.

The Asia and Pacific Alliance to Eliminate Viral Hepatitis (APAVH), a global partnership of the Asian Liver Center, US CDC and WHO, with support from the ZeShan Foundation, has been working with ministries of health to increase immunization coverage through innovative education and awareness projects. The organization has made commendable strides through country projects in China and the Lao People's Democratic Republic, and has developed comprehensive education and training materials to strengthen health-care workers' knowledge of hepatitis B.<sup>41</sup>

## World Hepatitis Day

In 2010, the World Health Assembly established 28 July as World Hepatitis Day, one of eight mandated public health days. The Western Pacific Region has since capitalized on this day by raising awareness of regional hepatitis B control initiatives. Other mass communication campaigns, such as World Immunization Week and World Health Day, provide additional opportunities to engage the community and increase awareness of the benefits of hepatitis B vaccination.

**In 2010, the World Health Assembly established 28 July as World Hepatitis Day, one of eight mandated public health days.**

40 Unpublished data presented at the 19th Meeting of the Technical Advisory Group on Immunization and Vaccine-Preventable Diseases in the Western Pacific Region, Manila, Philippines, 24–27 August 2010.

41 Education and Training. In: Asia and Pacific Alliance to Eliminate Viral Hepatitis (website). Palo Alto (CA): Asian Liver Center at Stanford University; 2014 (<http://apavh.org/our-work/education-and-training/>).

**Effective Strategies:**

1. Inform, educate and communicate with health-care providers in both public and private sectors to ensure awareness of the need for hepatitis B vaccination, including timely delivery of birth dose.
2. Educate parents, caregivers and the general community about the consequence of hepatitis B infection and the importance of immunization, using a range of information and education tools and materials, social media platforms and mass campaigns such as World Hepatitis Day and World Immunization Week.
3. Conduct periodic media workshops to ensure that the media understand that deaths following hepatitis B vaccination are usually not causally related to the vaccine.
4. Prepare AEFI communication response plans including AEFI committees to rapidly respond to any AEFI reports.

**Recommended indicators:**

- (1) Evidence of political commitment and allocation of appropriate funding to support hepatitis B immunization programmes.
- (2) Implementation of education and training of health-care workers that includes awareness of the importance of hepatitis B vaccination, how to prevent HBV transmission and key messages to convey to patients.
- (3) Level of vaccine acceptance by caretakers, as measured by caretaker surveys and reviews of positive and negative media coverage of hepatitis B vaccination.
- (4) Existence of AEFI communication response plans, including AEFI committees for rapid investigation and response.

**Further information:**

- Western Pacific Regional Office Hepatitis Website: <http://www.wpro.who.int/hepatitis/en/>
- Vaccine Safety Communication: Guidelines for Immunization Programme Managers/ National Regulatory Authority. Manila: WHO Regional Office for the Western Pacific; 2014.

**Hepatitis B advocacy materials:**

- (Brochure) Hepatitis B control in the Western Pacific Region: <http://www.wpro.who.int/hepatitis/resource/hepbcontrolbrochurelo.pdf?ua=1>
- (Video) Hepatitis B birth dose 30-second public service announcement [http://www2.wpro.who.int/internet/files/videos/wiw2014\\_HepBPSA\\_hires.html](http://www2.wpro.who.int/internet/files/videos/wiw2014_HepBPSA_hires.html)
- (Video) Controlling hepatitis B in the WHO Western Pacific Region: Achieving our goals: [http://www2.wpro.who.int/internet/files/videos/who\\_hepb\\_hires.html](http://www2.wpro.who.int/internet/files/videos/who_hepb_hires.html)

**Partner websites:**

- Asia and Pacific Alliance to Eliminate Viral Hepatitis: <http://apavh.org/>
- Asian Liver Center (Stanford University): <http://liver.stanford.edu/>
- US CDC – Hepatitis B: <http://www.cdc.gov/hepatitis/HBV/index.htm>
- ZeShan Foundation – Eradicating Hepatitis B: A Strategic Focus: [http://www.zeshanfoundation.org/index.php?route=ourprograms/our\\_program/getListing&current&programarea\\_id=14](http://www.zeshanfoundation.org/index.php?route=ourprograms/our_program/getListing&current&programarea_id=14)
- World Hepatitis Alliance: <http://www.worldhepatitisalliance.org/en/>
- Coalition to Eradicate Viral Hepatitis in Asia Pacific: <http://www.cevhap.org/index.php/en/>

## 7. MEASUREMENT OF PROGRAMME PERFORMANCE AND IMPACT



**The impact of hepatitis B immunization programmes should therefore be measured using nationally representative HBsAg seroprevalence surveys among children of 5 years or older born after the nationwide implementation of universal hepatitis B infant immunization.**

Evaluation of the progress toward achieving hepatitis control goals requires assessment of both programme performance and programme impact. Process indicators, such as coverage of the third dose and birth dose of hepatitis B vaccine, are useful for monitoring service delivery and highlighting priority areas and groups for increased attention. Programme impact is measured through prevalence of HBV infection among vaccinated cohorts.

The rationale for using seroprevalence of HBsAg among 5-year-old children as a marker for infection, rather than incidence of new infections or overt disease outcomes is that clinical symptoms in infected children often do not become apparent for several decades. The impact of hepatitis B immunization programmes should therefore be measured using nationally representative HBsAg seroprevalence surveys among children of 5 years or older born after the nationwide implementation of universal hepatitis B infant immunization (see Box 11).

The Western Pacific Region has established a verification process for documenting national achievement of the hepatitis B control goal.<sup>42</sup> In 2007, an independent, international panel—the Hepatitis B Expert Resource Panel (ERP) — was created in order to support the verification process and ensure a standard and independent mechanism for assessing achievement of control targets. Please see Chapter 8 for full details on the verification framework and the structure and function of ERP.

**Box 11. Can the seroprevalence data be from children older than 5 years?**

Yes. For example, if the HBsAg rate is demonstrated to be less than 1% among children aged 10 years in a country that introduced vaccine more than 10 years previously and has sustained high coverage with three doses of vaccine (that is, the coverage in last 10 years has remained consistently high), the country will be deemed to have achieved the regional goal of less than 1%. It is not necessary to have the seroprevalence data from children of exactly 5 years of age.

**Why shouldn't the seroprevalence data be from children younger than 5 years?**

Children younger than 5 years of age have not yet passed through the complete exposure period, and some who are currently uninfected and unimmunized may subsequently acquire chronic HBV infection. Therefore, seroprevalence estimates in children under 5 may underestimate the seroprevalence.

## 7.1 MONITORING PROGRAMME PERFORMANCE: VACCINE COVERAGE

As frequent serological surveys are not feasible, vaccine coverage rates can serve as a good interim proxy for programme performance. As vaccine efficacy is well known,<sup>43</sup> vaccine coverage data can provide an indication as to when countries should conduct a serosurvey. Vaccine coverage data can also identify areas of poor performance, where increased efforts and resources should be focused.

Monthly monitoring and mapping of vaccine coverage rates at all administrative levels (national, provincial and district) can help focus resources to address poor performing areas. Figure 5 is an example of a provincial vaccination coverage map from Cambodia. In the same vein, at the district level, monthly monitoring of vaccine coverage at the health-facility level, and allows managers to take timely programmatic action where coverage levels are below target.

42 Guidelines for certification of achievement of hepatitis B control goal in the Western Pacific Region. Manila: World Health Organization Regional Office for the Western Pacific; 2007.

43 Vaccine effectiveness, however, may be lower due to programmatic factors such as reduced vaccine potency due to freezing, delays in administration of birth dose, incorrect scheduling and drop-outs, and inequities in immunization coverage (with children at higher risk of HBV infection having less chance of getting vaccinated).



In order to maximize coverage and minimize resources required to carry out the survey, it is effective to integrate HBsAg testing with other serosurveys that may be conducted by other programmes (for example, lymphatic filariasis or yaws elimination programmes).

Where logistics and resources permit, additional age groups, such as 1-year-old children and mothers of sampled children, may be sampled to measure the impact on perinatal transmission. For countries that are conducting routine antenatal screening, regularly monitoring maternal seroprevalence rates and can be useful for programmatic action, by indicating areas where more intense control is required.

Guidelines for conducting a nationally representative seroprevalence survey, including guidance on sample size and the selection process, are available from WHO.<sup>45</sup>

### 7.2.1 Representativeness of the survey

The national prevalence of hepatitis B chronic infection is a key indicator of programme impact, and it is therefore very helpful for seroprevalence surveys to be nationally representative. If resources permit, surveys can be designed to provide representative subnational prevalence estimates as well. School-based surveys may be appropriate if more than 95% of children in the relevant age group attend school. If primary school enrolment is less than 95%, a community-based survey will provide a more representative estimate.

Convenience sampling (for example, testing of children admitted to a hospital) is not appropriate for generating representative prevalence estimates. However, convenience sampling may provide useful data in certain settings, such as small countries with only one or two health facilities catering to all children. If convenience sampling is used, it is important to explicitly address the likely direction of bias.

When attempting to measure low prevalence rates, careful attention is needed to ensure high accuracy. In order to generate a precise estimate, appropriate methodology must be employed and great care taken to ensure quality implementation according to the protocol. Potential issues that may lead to bias or reduced accuracy include non-random sampling, low participation rates, contamination of specimens, labelling errors, and misclassification of participants. Careful attention to survey design and close supervision of field-data collection and specimen handling are needed to avoid these problems. See Box 12.

#### Box 12. Steps to avoid sampling bias

- Ensure a complete nationwide sampling frame.
- For community surveys, use complete lists of children for second-stage sampling.
- Consider the timing of the survey and how seasonal residential and work patterns may affect the survey population coverage of the target population.
- Ensure high-quality training of data collectors and close supervision of field work.
- Attempt to maximize the response rate and collect demographic data on selected individuals who refuse to participate.

### 7.2.2 Appropriate sample size

For verification purpose, the sample size should be adequate to show with 95% confidence HBsAg prevalence of less than 1% with a precision of  $\pm 0.5\%$ .

Normally, with an expected seroprevalence of 1% and assuming a design effect of 2, a sample size of approximately 3000 will be required in order to achieve precision of  $\pm 0.5\%$ ,

45 WHO, Documenting the Impact of Hepatitis B Immunization: best practices for conducting a serosurvey (WHO/IBV/11.08); and WHO, Sample design and procedures for Hepatitis B immunization surveys (WHO/IBV/11.12)

When attempting to measure low prevalence rates, careful attention is needed to ensure high accuracy. Appropriate methodology must be employed and great care taken to ensure quality implementation according to the protocol.

with 95% confidence.

Large sample sizes may be difficult to achieve in countries and areas with smaller populations (and therefore very small birth cohorts). In these cases, either an entire birth cohort may be selected or special statistical methods can be used such as applying a finite population correction factor. Finite population corrections are appropriate in places where the sample size is more than 10% of the target population. For example, in 2012, Nauru had a total population of approximately 10,370 with a birth cohort of 365. Applying the finite population correction factor, a sample size of 359 was needed. Because this sample size was so close to the entire birth cohort, a census survey was chosen.

### 7.2.3 Laboratory testing

Serological assays are commercially available for all markers of HBV infection and the majority rely on enzyme-linked immunosorbent assay (ELISA) tests, which are quite sensitive and specific. The diagnosis of HBV infection and assessment of immunity to HBV requires laboratory detection of HBsAg and antibodies to hepatitis B surface antigen (anti-HBs), respectively. Testing for antibodies to hepatitis B core antigen (anti-HBc) may provide estimates of the resolved infection and natural immunity after infection in the past, besides providing estimates of lifetime risk of HBV infection (see Table 2).

Where possible, it is advantageous to collect blood specimens for ELISA laboratory testing because the accuracy (sensitivity and specificity) is higher than for rapid tests, and additional tests can be conducted to determine past hepatitis B infection, hepatitis B genotyping, and DNA testing (see Table 2 and Box 13).

The minimum requirement for the verification process is valid estimates of HBsAg prevalence. Therefore, in areas lacking laboratory capacity and in other resource-constrained settings, the testing may be done with rapid field tests (also called point-of-care tests), which can only detect the presence of HBsAg. Rapid tests offer several advantages for undertaking a serosurvey: they are low cost; they require only minimal training and laboratory infrastructure; they require only a drop of blood as opposed to venepuncture; they have no cold chain requirements; and there is no specimen handling. They also offer immediate results, with the potential for counselling, referral and immunization of contacts. Only tests that have been evaluated for their sensitivity and specificity in field settings should be used.<sup>46,47</sup>

**Table 2. Serological markers of hepatitis B infection and immunity**

Markers	Interpretation
HBsAg (+)	Chronic infection, if persistent for more than six months
HBeAg (+)	Marker of increased HBV infectivity (high likelihood of perinatal transmission)
Anti-HBc (+)	Past or present infection
HBsAg (-) and Anti-HBc (+)	Immune as a result of past infection, no chronic infection
Anti-HBs (+) and Anti-HBc (-)	Immune as a result of vaccination

46 See Tables S.1 and S.2 in Documenting the Impact of Hepatitis B Immunization: best practices for conducting a serosurvey (WHO/IBV/11.08) for field sensitivities and specificities of commercially available rapid HBsAg tests.

47 Hepatitis B surface antigen assays: operational characteristics (Phase I). Report 1. Geneva: World Health Organization; 2001 (WHO/BCT/BTS/01.4, [www.who.int/diagnostics\\_laboratory/evaluations/en/hep\\_B\\_rep1.pdf](http://www.who.int/diagnostics_laboratory/evaluations/en/hep_B_rep1.pdf)).

**Box 13. Additional questions that can be answered through serosurveys**

The minimum requirement for the verification process is valid estimates of HBsAg prevalence, however where resources allow, serosurveys can be used to collect additional useful information, such as:

- prevalence of HBeAg among pregnant women, indicating higher infectivity;
- level of perinatal transmission;
- genotyping of HBV in circulation; and
- prevalence of HBV variants and “escape mutants”.

**Strategies:**

1. Assess programme performance: Monitor immunization coverage rates (for third dose, for birth dose administered within 24 hours, and for birth dose given after 24 hours but prior to first combination dose), and establish systems to monitor birth dose coverage for health facility and home deliveries.
2. Conduct HBsAg seroprevalence surveys to measure impact of the hepatitis B immunization programme.
3. Verify the achievement of reaching control targets. See Chapter 8 for verification framework.
4. Sustain the gains: post-verification, continue to monitor and maintain high and timely coverage. Develop and strive towards a goal beyond 2017, such as interruption of perinatal transmission.

**Recommended indicators:**

- (1) Seroprevalence of HBsAg among children 5 years or older.
- (2) Percentage of infants vaccinated with three doses of vaccine by age 1 year at national level and at each subnational/district level.
- (3) Percentage of newborn infants given timely birth dose (within 24 hours of birth) at national level and at each subnational/district level. If possible, it is helpful to monitor birth dose coverage separately for health-facility births and home births.
- (4) Percentage of newborn infants given any birth dose (>24 hours, up until the time of the first combination dose), at national level and at each subnational/district level. If possible, it is helpful to monitor birth dose coverage separately for health-facility births and home births.

**Further information:**

- Documenting the Impact of Hepatitis B Immunization: best practices for conducting a serosurvey (WHO/IVB/11.08): [http://whqlibdoc.who.int/hq/2011/WHO\\_IVB\\_11.08\\_eng.pdf](http://whqlibdoc.who.int/hq/2011/WHO_IVB_11.08_eng.pdf)
- Sample design and procedures for Hepatitis B immunization surveys: A companion to the WHO cluster survey reference manual (WHO/IVB/11.12): [http://whqlibdoc.who.int/hq/2011/WHO\\_IVB\\_11.12\\_eng.pdf](http://whqlibdoc.who.int/hq/2011/WHO_IVB_11.12_eng.pdf)
- Immunization coverage cluster survey - Reference manual (WHO/IVB/04.23): [http://whqlibdoc.who.int/hq/2005/WHO\\_IVB\\_04.23.pdf](http://whqlibdoc.who.int/hq/2005/WHO_IVB_04.23.pdf)
- Training for mid-level managers (MLM), module 7: The EPI coverage survey (WHO/IVB/08.07): [http://whqlibdoc.who.int/hq/2008/WHO\\_IVB\\_08.07\\_eng.pdf](http://whqlibdoc.who.int/hq/2008/WHO_IVB_08.07_eng.pdf)



## 8. VERIFICATION FRAMEWORK



## 8.1 VERIFICATION CRITERIA

In 2007, the Western Pacific Region established a verification<sup>48</sup> process for documenting national achievement of the hepatitis B control goal of less than 1% hepatitis B chronic infection prevalence among 5-year-old children.<sup>49</sup> The verification of achievement of the goal is based on serological surveys of HBsAg seroprevalence among children 5 years or older, born after the start of a nationwide infant vaccination programme.

In order to initiate the verification process, a country must have:

- (1) at least one nationally representative serological survey documenting HBsAg rates among children 5 years or older, with point estimates indicating target prevalence levels (less than 1%) have been reached; and
- (2) at least five years of high hepatitis B vaccination coverage, preferably beyond the target threshold levels.

## 8.2 VERIFICATION THRESHOLDS AND INDICATORS

### 8.2.1 Seroprevalence of HBsAg of less than 1%

The key requirement for verification of achievement of control goals is data indicating seroprevalence of HBsAg of less than 1%, among children 5 years or older. Point estimates should be within  $\pm 0.5\%$  accuracy, with 95% confidence. However, these thresholds are for guidance only; smaller countries such as many Pacific island countries and areas may have very small birth cohorts and therefore may have difficulty achieving adequate sample sizes to achieve these statistical thresholds. Every country should undertake at least one nationally representative survey of children at least 5 years old, born after the implementation of a universal infant vaccination programme.

### 8.2.2 Criteria for validity of a serosurvey for the purpose of verification

The serosurvey should be representative of the country, should have an appropriate sample size, and should utilize quality testing assays and laboratory procedures. A report of the serologic survey must be submitted for verification and should include the following information:

- methods, including sampling methods (target ages, geographic areas, and sampling frame) time period of participant enrolment/specimen collection, exclusion criteria if any, laboratory test used, and testing algorithm;
- results, including HBsAg prevalence and confidence intervals by age and if possible by gender, geographic region, race/ethnicity, urban/rural, socioeconomic status, vaccination status including birth dose within or after 24 hours of birth, and if possible, a comparison of characteristics between refusals and participants of the study; and
- discussion, including whether the survey represents the country's population, especially with regards to possible groups at high risk of infection (that is, certain minority groups) and study limitations.

48 The terminology for the evaluation process for hepatitis B control was changed from "certification" to "verification" in 2011, for consistency with other vaccine-preventable disease goals in the Region. The term "certification" is used for eradication initiatives (such as smallpox and polio), where a country/region can be certified as disease-free.

49 Guidelines for certification of achievement of hepatitis B control goal in the Western Pacific Region. Manila: World Health Organization Regional Office for the Western Pacific; 2007; and Country instructions for verifying achievement of hepatitis B control goals in the WHO Western Pacific Region. Manila: World Health Organization Regional Office for the Western Pacific; 2011.

### 8.2.3 Vaccination coverage

Even though vaccine coverage data will not be used as primary criteria for verification, the verification panel will assess the vaccine coverage data carefully and make recommendations for increasing coverage and achieving better control.

If a country achieves less than 1% HBsAg seroprevalence among cohorts 5 years or older, but recent vaccine coverage levels are below recommended targets, the country may still be verified as having achieved the regional goal, provided the country presents plans to increase vaccine coverage levels in order to maintain verification status.

The targets for key vaccination-coverage indicators are as follows:

- at least 95% of infants immunized with three doses of hepatitis B vaccine by age 1 year at national level and at least 85% at each subnational/district level; and
- at least 95% of newborn infants given timely birth dose within 24 hours of birth at national level and at least 85% at each subnational/district level.

### 8.2.4 Sources of vaccine coverage data

The verification panel will want to corroborate the routinely collected administrative coverage data with data from at least one population-based survey collected in the same period. As far as possible, the estimates from the administrative data should be within  $\pm 5\%$  points of the estimates from the household survey in order to be acceptable.

In the absence of such survey data from the past five years, the verification panel may look for other proof of the quality of the administrative data, especially in countries where the quality of vaccine coverage data are perceived to be poor. Forms of proof can include data-quality audit reports or other reports from data-quality assessments if carried out in the past five years. The score of the data-quality audit should not be less than 0.80 for the administrative estimates to be acceptable.

### 8.2.5 Additional surveillance data (if available)

Trend data on acute hepatitis incidence, especially among children less than 10 years of age, are rarely available for most countries. Similar issues apply to data on morbidity and mortality due to chronic hepatitis B infection. Hence, these data, if available, will be used to supplement vaccine coverage and seroprevalence data but will not be a mandatory requirement for the verification process.

## 8.3 STRUCTURE AND FUNCTION OF ERP

The Expert Resource Panel consists of 10–15 members, appointed by the WHO Regional Director for the Western Pacific, and representing an independent, international body of expertise. Members of the ERP serve terms of two years, with the possibility of renewal. When requests for verification of reaching the hepatitis B control targets are made by Member States, three-member verification panels carry out the review process.

The terms of reference for ERP members are as follows:

- (1) Serve in an honorary capacity to advise on the status of hepatitis B control in Member States in the Western Pacific Region.
- (2) Serve on a three-person verification panel comprised of ERP members when a request is received from a Member State for verification of reaching the hepatitis B control targets, which may involve reviewing documents submitted by the country and/or visiting the Member State.

- (3) Advise on issues related to hepatitis B control and achievement of the regional control goals.

The ERP holds annual meetings and communicates as needed by email and teleconference to monitor and facilitate progress towards achieving hepatitis B control goals in the Region.

## 8.4 VERIFICATION PROCEDURE

The verification process is initiated at the request of the national health authorities, once the country has met the threshold criteria for verification. A formal request is submitted to the Regional Office with supporting documents that include:

- report of a nationally representative serosurvey conducted among children 5 years or older, with detailed methodology, results and discussion; and
- vaccine coverage data, reported in the past five years, for all vaccine coverage indicators.

Detailed instructions for preparation of the verification package, including the verification report form, are available on the WHO Regional Office for the Western Pacific website.<sup>50</sup> The report form can also be found in Annex 3.

A three-member verification panel will be convened to carry out a detailed desk-review of the vaccination coverage data and the seroprevalence data, as submitted by the country in the verification package. A field visit to the country will be undertaken, if needed.

Each country will be reviewed on a case-by-case basis, taking into account factors including demographics and historical chronic HBV rates, and the verification panel may relax or tighten some of the requirements for verification.

The verification panel will prepare a report detailing whether the country has or has not met the verification thresholds, the reasons for its finding, and follow-up recommendations. The panel recommendations will be circulated to all ERP members for review and input before a final decision is taken by consensus. The entire verification process takes three to four months.

## 8.5 POST-VERIFICATION

Once verified, countries are encouraged to monitor and maintain high and timely coverage to ensure that gains are sustained. The ERP will review post-verification vaccination performance on an annual basis.

Strong political commitment and sufficient financing are needed to sustain the low hepatitis B transmission through robust routine immunization programmes, action plans for improving coverage in poor-performing districts, and increasing access to timely birth dose.

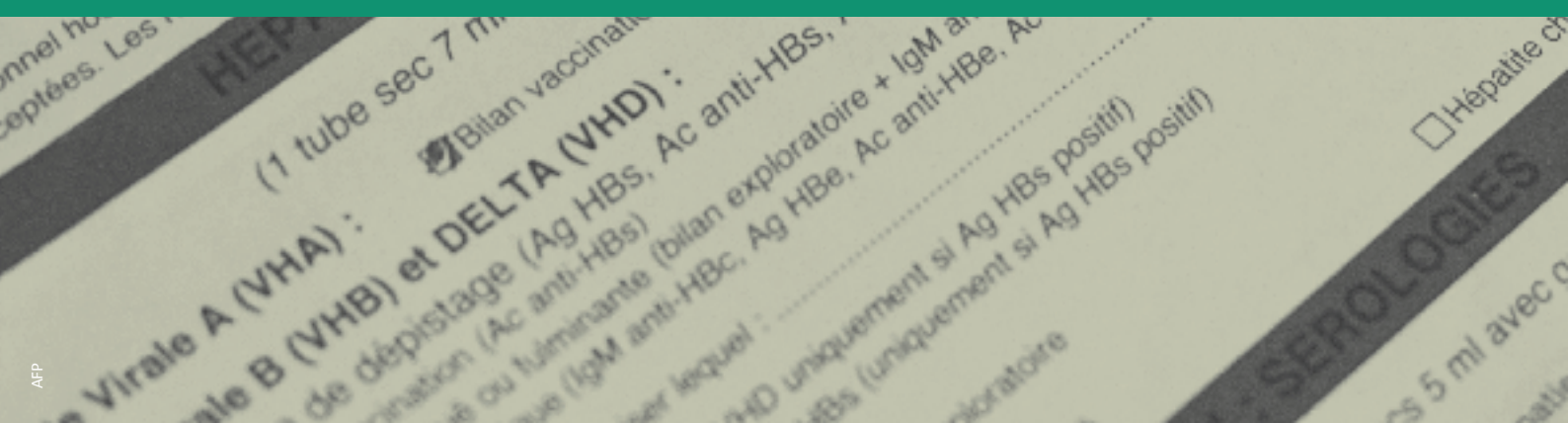
### Further information:

- Guidelines for certification of achievement of hepatitis B control goal in the Western Pacific Region, 2007: <http://www.wpro.who.int/immunization/documents/docs/HepBControlCertifGuidelines.pdf>
- WHO Western Pacific Regional hepatitis B control verification: Instructions: <http://www.wpro.who.int/hepatitis/hepbverificationguidelines.pdf>

50 WHO Western Pacific Regional hepatitis B control verification: Instructions. Manila: World Health Organization Regional Office for the Western Pacific (<http://www.wpro.who.int/hepatitis/hepbverificationguidelines.pdf>).



## 9. SELECTED RESOURCES AND GUIDANCE DOCUMENTS



**Hepatitis B vaccine:**

- WHO position paper on hepatitis B vaccines, *Wkly Epidemiol Rec.* 2009 Oct 1;84(40): 405–19, available online: <http://www.who.int/wer/2009/wer8440.pdf>.
- Introducing hepatitis B vaccine into national immunization services (WHO/V&B/01/28): [http://whqlibdoc.who.int/hq/2001/WHO\\_V&B\\_01.28.pdf](http://whqlibdoc.who.int/hq/2001/WHO_V&B_01.28.pdf)
- Introduction of hepatitis B vaccine into childhood immunization services. Management guidelines, including information for health workers and parents (WHO/V&B/01.31): [http://whqlibdoc.who.int/hq/2001/WHO\\_V&B\\_01.31.pdf](http://whqlibdoc.who.int/hq/2001/WHO_V&B_01.31.pdf).
- The Immunological Basis for Immunization Series: Hepatitis B (WHO, 2012): [http://apps.who.int/iris/bitstream/10665/77755/1/9789241504751\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/77755/1/9789241504751_eng.pdf)

**Birth dose coverage:**

- Practices to improve coverage of the hepatitis B birth dose vaccine (WHO/IVB/12.11): [http://apps.who.int/iris/bitstream/10665/78616/1/WHO\\_IVB\\_12.11\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/78616/1/WHO_IVB_12.11_eng.pdf)
- Consultation on Improving and Monitoring Hepatitis B Birth Dose Vaccination (WHO, 2012): [http://www.wpro.who.int/entity/immunization/documents/consultation\\_HepB\\_birthdose\\_June2012\\_mtgprpt.pdf](http://www.wpro.who.int/entity/immunization/documents/consultation_HepB_birthdose_June2012_mtgprpt.pdf)
- Preventing Mother-to-child Transmission of Hepatitis B: Operational field guidelines for delivery of the birth dose of hepatitis B vaccine (WHO, 2006): <http://www.wpro.who.int/immunization/documents/docs/HepBOperationalFieldGuidelines.pdf>

**Population surveys (hep B focus):**

- Documenting the Impact of Hepatitis B Immunization: best practices for conducting a serosurvey (WHO/IVB/11.08): [http://whqlibdoc.who.int/hq/2011/WHO\\_IVB\\_11.08\\_eng.pdf](http://whqlibdoc.who.int/hq/2011/WHO_IVB_11.08_eng.pdf)
- Sample design and procedures for Hepatitis B immunization surveys: A companion to the WHO cluster survey reference manual (WHO/IVB/11.12): [http://whqlibdoc.who.int/hq/2011/WHO\\_IVB\\_11.12\\_eng.pdf](http://whqlibdoc.who.int/hq/2011/WHO_IVB_11.12_eng.pdf)

**Population surveys (general):**

- Immunization coverage cluster survey - Reference manual (WHO/IVB/04.23): [http://whqlibdoc.who.int/hq/2005/WHO\\_IVB\\_04.23.pdf](http://whqlibdoc.who.int/hq/2005/WHO_IVB_04.23.pdf).
- Training for mid-level managers (MLM), module 7: The EPI coverage survey (WHO/IVB/08.07): [http://whqlibdoc.who.int/hq/2008/WHO\\_IVB\\_08.07\\_eng.pdf](http://whqlibdoc.who.int/hq/2008/WHO_IVB_08.07_eng.pdf)

**Verification guidelines:**

- Guidelines for Certification of Achievement of Hepatitis B Control Goal in the Western Pacific Region, 2007: <http://www.wpro.who.int/immunization/documents/docs/HepBControlCertifGuidelines.pdf>
- WHO Western Pacific Regional hepatitis B control verification: Instructions (update to guidelines and report template): [http://www.wpro.who.int/immunization/documents/HepBVerificationPackage\\_20110521v4.pdf](http://www.wpro.who.int/immunization/documents/HepBVerificationPackage_20110521v4.pdf)

**Health-care workers:**

- Vaccinating health-care workers against hepatitis B (WHO, 2012): <http://www.wpro.who.int/immunization/documents/docs/HepBVaccinatingHCW.pdf>

**Vaccine management:**

- WHO Aide-memoire Preventing Freeze Damage to Vaccines (WHO/IVB/07.09): [http://whqlibdoc.who.int/hq/2007/WHO\\_IVB\\_07.09\\_eng.pdf](http://whqlibdoc.who.int/hq/2007/WHO_IVB_07.09_eng.pdf)
- Temperature sensitivity of vaccines (WHO/IVB/06.10): [http://whqlibdoc.who.int/hq/2006/WHO\\_IVB\\_06.10\\_eng.pdf](http://whqlibdoc.who.int/hq/2006/WHO_IVB_06.10_eng.pdf)

**Additional information on hepatitis B is available on the following websites:**

- [www.cdc.gov/ncidod/diseases/hepatitis/b/index.htm](http://www.cdc.gov/ncidod/diseases/hepatitis/b/index.htm)
- [www.immunize.org/hepb/index.htm](http://www.immunize.org/hepb/index.htm)
- [www.hepnet.com/hepb.html](http://www.hepnet.com/hepb.html)
- [www.hepb.org](http://www.hepb.org)
- [www.hepatitisb.org](http://www.hepatitisb.org)
- [www.path.org/vaccineresources/files/HBV\\_training\\_module\\_CVP.pdf](http://www.path.org/vaccineresources/files/HBV_training_module_CVP.pdf)

## ANNEX 1: HEPATITIS B VIRUS

### History

Hepatitis transmitted through serum was first documented during a smallpox immunization campaign in 1883. McCallum proposed the term hepatitis B for “serum” hepatitis in 1947, as opposed to hepatitis A, spread by the faecal-oral route. The hepatitis B surface antigen (HBsAg) was first identified in the liver of an Australian Aborigine in 1967 (initially called Australia antigen).

### Virology

Hepatitis B virus (HBV) is a DNA virus with a core antigen (HBcAg) surrounded by a coat containing surface antigen (HBsAg). The immune response to HBsAg provides the basis for immunity against HBV. Antibodies to HBcAg (anti-HBc) indicate infection—IgM anti-HBc indicates recent infection and usually disappears within six months, while IgG anti-HBc persists for life and indicates past infection. Antibodies to HBsAg (anti-HBs) only appear after clearance of HBsAg or after immunization. The presence of HBsAg for more than six months is defined as chronic HBV infection (or carriage). The presence of a third antigen, HBeAg, indicates a high degree of infectivity (that is, actively replicating virus).

### Transmission

HBV enters the body parenterally or through small breaks in the skin or mucosal linings. The virus is found in the blood and body fluids of acute or chronically infected individuals. Blood and fluids become less infectious as they dry on exposure to air. The greatest spread is between young children, probably related to contact with skin sores and small breaks in the skin, and from household contacts (including adults). The virus is also passed from mother to baby as a result of exposures to blood or vaginal fluid during childbirth. The baby of an HBsAg-positive mother has a 70–90% risk of infection if the mother is HBeAg-positive, and about a 10% risk if she is HBeAg-negative. Providing post-exposure prophylaxis by immunizing the child with a first dose of hepatitis B vaccine within 24 hours of birth reduces the risk by 70–95%. Studies suggest that breastfeeding by an HBsAg-positive mother does not increase an infant’s risk for acquisition of HBV infection.<sup>1</sup>

Sexual contact, non-sterile (that is, shared or re-used without sterilization) injections, and any other way of passing body fluids can lead to infection. HBV is not spread through the air or in food. The incubation period before seroconversion varies from six weeks to six months, and is usually three to four months.

### Outcomes of infection

The initial infection is referred to as acute HBV infection; it may be either symptomatic (acute hepatitis B) or asymptomatic. The outcomes of acute HBV infection are either (1) chronic HBV infection (carriage) or (2) immunity.

**Chronic HBV infection (carriage):** Usually with no symptoms, the virus remains in the liver, where it eventually (after decades) can cause liver cancer or cirrhosis, leading to premature death in up to 25% of chronically infected persons. The major HBV-related disease burden is from these consequences of chronic infection.

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<sup>1</sup> Beasley RP, Stevens CE, Shiao IS, Meng HC. Evidence against breast-feeding as a mechanism for vertical transmission of hepatitis B. *Lancet*. 1975;2(7938):740–1.

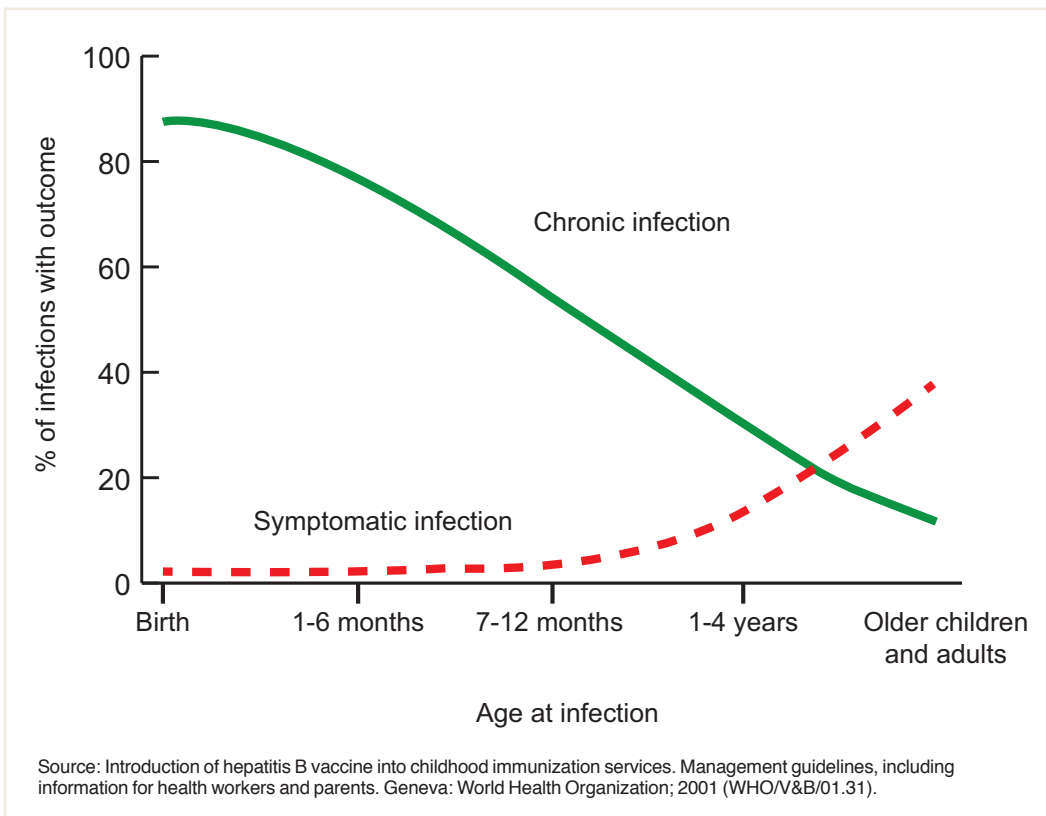
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**Acute HBV infection:** An acute illness lasting several weeks, with loss of appetite, weakness, nausea, vomiting, abdominal pain, jaundice (yellow skin or eyes), dark urine, skin rashes and joint pain. The person usually recovers with no long-term effects, but 1–2% will die from fulminant hepatitis (mortality increases with age).

The age at which a person becomes infected with HBV is the main factor determining the outcome (see Figure A1.1). The risk of chronic HBV infection drops from about 90% in the first six months of life, to about 30% by the age of 5 years and 10% by the age of 15 years.<sup>2</sup> It is unusual (2–5%) for those infected in later adult life to develop chronic infection. Fewer than 10% of children less than 5 years old and only 30–50% of adults develop symptomatic acute hepatitis B after infection.<sup>3</sup>

**Figure A1.1. Outcome of HBV infection by age at infection**



### Escape mutants

As with any virus, mutations occur in the hepatitis B virus. Over time, it is possible for variants of the virus to arise that are not protected by the vaccine. These are known as “escape mutants”. Despite apparent increases in reports, the prevalence of HBV escape mutants is low and it is not yet clear whether these escape mutants are of public health importance<sup>4</sup>. Ongoing monitoring is needed to assess their implications.

2 Edmunds WJ, Medley GF, Nokes DJ, Hall AJ, Whittle HC. The influence of age on the development of the hepatitis B carrier state. *Proc Biol Sci.* 1993;253(1337):197–201.

3 McMahon BJ, Alward WL, Hall DB, Heyward WL, Bender TR, Francis DP, et al. Acute hepatitis B virus infection: relation of age to the clinical expression of disease and subsequent development of the carrier state. *J Infect Dis.* 1985;151(4):599–603.

4 Bian T, Yan H, Shen L, Wang, F, Zhang S, Cao, Y, et al. Change in hepatitis B virus large surface antigen variant prevalence 13 years after implementation of a universal vaccination programme in China. *J Virol.* November 2013;87(22):12196–206.

## ANNEX 2: HEPATITIS B VACCINE

### History and types of vaccine

Hepatitis B surface antigen (HBsAg) is the main component of hepatitis B vaccine. Plasma-derived hepatitis B vaccine, available from 1982, uses HBsAg from the blood of people with chronic HBV infection. In 1986, recombinant vaccines were introduced, using HBsAg derived from yeast cells or mammalian cells that are genetically modified by inserting (recombining) the gene coding for HBsAg protein. Recombinant vaccine is currently the most commonly used vaccine type. In both types of vaccines, the HBsAg is joined to an aluminium salt to increase its immunogenicity. The vaccine can also contain a preservative (for example, thimerosal)

In 2004, WHO recommended universal provision of three doses of hepatitis B vaccine for infants worldwide.<sup>5</sup> By the end of 2012, 181 (93%) of WHO Member States globally had introduced the three-dose schedule. In 2009, WHO recommended universal birth dose vaccination within 24 hours worldwide.<sup>6</sup> By the end of 2012, 94 (48%) of WHO Member States globally had introduced the birth dose.

### Combination vaccines

Hepatitis B vaccine is now available as tetravalent (DPT-HepB) and pentavalent vaccine (DPT-HepB-Hib), reducing the number of injections required to complete the Expanded Programme on Immunization (EPI) vaccination schedule. However, the birth dose of hepatitis B vaccine can be given only as monovalent HepB vaccine, as DTP is not recommended before the age of four weeks. Currently, the majority of countries in the Region are using combination vaccines in their national immunization schedules.

### Vaccine efficacy

Hepatitis B vaccine is remarkably effective. Clinical trials in high-risk groups have shown immunogenicity of 85–95% and virtually complete protection in those who developed antibody levels of  $\geq 10$  mIU/ml (considered the protective level).

At least 95% of infants, children and adolescents develop protective antibody levels after three doses of vaccine. The response rate drops with age from 90% for adults under 40 years to about 70% for those aged 60 years.

### Vaccine schedules

Hepatitis B vaccine has been shown to be immunogenic using a wide range of schedules.<sup>7</sup> In general, three doses given at intervals of at least four weeks (but not more than two months between the first and second doses) are recommended. Please refer to Table 1 in Chapter 3 for the recommended schedules in the Western Pacific Region.

Although antibody levels decline after immunization, immune memory is maintained and booster doses do not appear to be needed to maintain immunity for the duration of the

5 WHO. Hepatitis B vaccines. *Wkly Epidemiol Rec.* 9 July 2004;79:253–64.

6 WHO. Hepatitis B vaccines. *Wkly Epidemiol Rec.* 2 October 2009;84:405–20.

7 West DJ, Calandra GB, Hesley TM, Ioli V, Miller WJ. Control of hepatitis B through routine immunization of infants: the need for flexible schedules and new combination vaccine formulations. *Vaccine.* 1993;11 Suppl 1:S21–7.

follow-up studied to date.<sup>8</sup> Therefore, booster doses are not currently recommended by WHO and other experts.<sup>9</sup>

### **Vaccine safety**

Anaphylaxis is the only known serious reaction to hepatitis B vaccine. However, the risk of anaphylaxis is estimated at 1 per 600 000 doses. Even minor reactions (for example, fever and local inflammation) are relatively rare.

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8 West DJ, Calandra GB. Vaccine-induced immunologic memory for hepatitis B surface antigen: implications for policy on booster vaccination. *Vaccine*. 1996;14(11):1019–27.

9 European Consensus Group on Hepatitis B Immunity. Are booster immunisations needed for lifelong hepatitis B immunity? *Lancet*. 2000;355:561–5.

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## ANNEX 3: HEPATITIS B VACCINATION COVERAGE AND CHRONIC INFECTION ESTIMATES

2017 Goal Category	Country / Area	Timely birth dose (%)							Three-dose (%)							HBsAG prevalence estimate+
		'07	'08	'09	'10	'11	'12	'13	'07	'08	'09	'10	'11	'12	'13	
Verified  Has met the goal (n=11)	Australia	NR	NR	NR	NR	NR	NR	NR	94	94	92	92	92	92	91	0.2%
	Brunei Darussalam	NR	100	100	96	95	95	100	97	96	96	96	93	99	98	0.1%
	China	86	91	93	92	95	96	96	92	95	99	99	99	99	100	0.9%
	Cook Islands	100	100	100	99	97	97	98	99	99	82	99	93	98	98	0.0%
	Hong Kong SAR (China)	95	95	96	95	95	100	95	95	95	96	95	95	95	95	0.8%
	Macao SAR (China)	100	100	100	NR	100	100	100	90	91	92	NR	94	94	93	0.0%
	Malaysia	90	99	95	95	98	NR	87	90	95	95	96	97	98	96	0.3%
	Mongolia	87	94	98	95	96	97	97	98	96	97	96	99	99	98	0.5%
	New Zealand	NA	NA	NA	NA	NA	NA	NA	88	90	93	90	95	93	93	0.2%
	Palau	100	67	100	100	100	100	100	91	92	69	80	91	89	99	0.0%
	Republic of Korea	94	94	95	95	NR	NR	NR	91	94	94	94	99	99	99	0.2%
Likely  Has prevalence data indicating that goal may be met (n=3)	American Samoa	100	100	100	NR	NR	gNR	NR	90	89	NR	NR	NR	NR	NR	0.2%
	Singapore	99	NR	NR	NR	NR	NR	NR	95	96	97	96	96	96	NR	0.0%
	Wallis and Futuna	100	NR	100	100	100	100	NR	91	NR	100	NR	NR	100	NR	0.4%
Likely Serosurvey planned or ongoing (n=14)	French Polynesia	100	NR	NR	NR	NR	NR	NR	99	NR	99	99	99	99	NR	ND
	Fiji	81	100	NR	NR	61	100	99	99	99	99	99	99	99	98	ND
	Marshall Islands	90	NR	98	99	74	85	70	93	97	99	97	89	80	41	ND
	Northern Mariana Islands	97	100	100	100	100	98	NR	80	96	93	83	97	76	NR	ND
	Tonga	100	100	99	99	100	100	100	99	98	99	99	99	95	100	ND
	Kiribati	58	59	52	63	66	82	84	96	83	86	91	95	94	95	ND
	Samoa	98	81	75	91	100	96	91	69	38	72	87	91	99	95	ND
	Guam	100	99	100	NR	NR	100	100	NR	NR	NR	NR	NR	38	NR	ND
	Federated States of Micronesia	86	90	88	80	81	81	69	90	89	89	88	83	82	83	ND
	Nauru	100	100	100	100	NR	100	NR	99	99	99	99	99	79	NR	ND
	New Caledonia	99	99	99	99	99	98	98	98	98	98	98	98	93	93	ND
	Niue	99	100	100	55	100	100	100	98	99	99	99	98	98	100	ND
	Tokelau	100	100	100	100	100	56	33	100	97	100	98	98	100	98	ND
Tuvalu	100	100	100	99	98	100	NR	97	99	91	89	96	97	NR	ND	
Pending  Program improvements required (n=8)	Papua New Guinea	29	27	27	35	31	35	37	59	56	62	56	61	63	68	ND
	Cambodia	25	46	55	57	68	65	58	82	91	92	92	94	95	92	3.5%
	Japan**	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	<1%
	Lao People's Democratic Republic	6	9	20	NR	NR	NR	NR	50	61	67	74	78	79	87	1.7%
	Vietnam	27	24	40	21	55	76	56	67	87	94	88	95	97	59	1.6%
	Philippines	9	21	34	37	40	35	44	87	88	85	77	76	70	94	ND
	Solomon Islands	83	80	45	62	75	59	58	79	77	81	79	88	90	83	ND
	Vanuatu	79	73	55	63	73	79	77	59	59	59	59	59	59	75	ND

\* 2013 data are preliminary

\*\* Japan has less than 1% estimated hepatitis B chronic infection prevalence among children but does not have a policy of universal infant vaccination with hepatitis B containing vaccine.

Data sources: WHO UNICEF Estimates of national immunization coverage when available (coverage of three doses of hepatitis B vaccine among member states); else WHO/UNICEF Joint Reporting Form

Note: There are 37 Member States; Pitcairn Island not represented here. NR= No Report; NA = Not applicable

+ Recent nationally representative data of prevalence among children



