Preventing Mother-to-Child Transmission of Hepatitis B

OPERATIONAL FIELD GUIDELINES for Delivery of the Birth Dose of Hepatitis B Vaccine

World Health Organization
Western Pacific Region
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World Health Organization
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 Worldwide, an estimated 350 million people have chronic hepatitis B infections. In spite of having only 28% of the global population, the Western Pacific Region bears a disproportionate burden of hepatitis B-related mortality and morbidity, accounting for almost half of all chronic liver infections worldwide. With an estimated 160 million chronic carriers living in the Region, hepatitis B is responsible for almost 890 deaths per day, a mortality rate comparable to that of tuberculosis. With few exceptions, most countries were estimated to have a chronic carriage rate of more than 8% before the introduction of vaccination. Hepatitis B control is, therefore, an important regional public health priority.

Universal childhood immunization with three doses of hepatitis B vaccine in the first year of life has proven to be the most effective strategy to control hepatitis B. In 2002, the Western Pacific became the first WHO Region to achieve the distinction of having hepatitis B immunization included in the national immunization programmes (NIPs) of all its Member States. Striving to build upon the gains achieved in immunization systems during the poliomyelitis eradication initiative, the Region has adopted hepatitis B control through universal childhood immunization as one of the pillars for strengthening immunization service delivery systems. In September 2005, the Western Pacific became the first WHO Region to set a time-bound goal of reducing chronic hepatitis B infection rates to less than 2% among five-year-old children by 2012.

In the Western Pacific Region, mother-to-child transmission at birth plays a very important role in hepatitis B epidemiology. Approximately 3% to 5% of infants born in the Region will acquire chronic hepatitis B infection at birth if not immunized immediately after the delivery. Hence, timely delivery of the first dose of the vaccine within 24 hours of birth, and thus prevention of mother-to-child transmission, is as critical to reducing the spread of the disease as maintaining overall high coverage with three doses of hepatitis B vaccine.
While increasing coverage with three doses of hepatitis B vaccine depends on the overall strengthening of routine systems, provision of the first dose within 24 hours of birth provides special challenges, especially in countries where a substantial proportion of births occur at home, unsupervised by any trained health worker. Despite those challenges, the clear need for the birth-dose delivery of hepatitis B vaccine also provides an invaluable opportunity to link immunization delivery systems with maternal health care systems, and may have the positive effect of increasing women’s access to trained maternity care — an indicator to measure progress towards reduction of maternal mortality — an important Millennium Development Goal.

These guidelines for developing and implementing operational strategies for increased coverage of the first dose of hepatitis B vaccine within 24 hours of birth are being released in this field test version so that there may be an opportunity to learn from Member States’ experiences. Please share your experiences with the Western Pacific Regional Office so that we can work together to achieve another historic milestone, that of reducing the hepatitis B burden and eradicating the disease in the coming years.
Acknowledgements

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Finally, we are extremely grateful to our national counterparts from the Member States in the Western Pacific Region, who arranged many field visits to the health facilities to review the hepatitis B birth dose programme. The field visits provided invaluable insights and contributed substantially to the development of ideas for this manuscript.
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>AntiHBs</td>
<td>Antibodies against hepatitis B surface antigen, the presence of which indicates protection (either following infection or immunization).</td>
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<tr>
<td>AntiHBc</td>
<td>Antibodies against the hepatitis B core antigen.</td>
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<tr>
<td>Cirrhosis</td>
<td>Chronic infection and scarring of the liver as a result of chronic inflammation of liver cells.</td>
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<tr>
<td>Chronic Carrier</td>
<td>Person with long-term HBV infection, defined as persistence of HbsAg in the blood for more than six months.</td>
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<tr>
<td>DTP</td>
<td>Diphtheria-tetanus-pertussis vaccine.</td>
</tr>
<tr>
<td>DTP-HepB</td>
<td>A combination vaccine of DTP with hepatitis B vaccine.</td>
</tr>
<tr>
<td>EPI/NIP</td>
<td>Expanded Programme on Immunization/National Immunization Programme.</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>A liver infection caused by the hepatitis B virus. Clinically indistinguishable from other causes of viral hepatitis.</td>
</tr>
<tr>
<td>HBcAg</td>
<td>Hepatitis B core antigen, a protein found in the core of the HBV.</td>
</tr>
<tr>
<td>HBeAg</td>
<td>Hepatitis B ‘e’ antigen, the presence of which implies active viral replication, thus making it a marker of greater infectivity in chronic infection.</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Hepatitis B surface antigen: a protein from the virus’s coat. Its presence in the blood indicates current infection (acute or chronic). The immune response to HBsAg provides the basis for immunity against HBV.</td>
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<tr>
<td>HBV</td>
<td>Hepatitis B Virus, a double-shelled DNA virus of the <em>Hepadnaviridae</em> family.</td>
</tr>
<tr>
<td><strong>HCC</strong></td>
<td>Hepatocellular carcinoma, or primary liver cancer – a major complication of chronic HBV infection; usually fatal.</td>
</tr>
<tr>
<td><strong>HepB3</strong></td>
<td>The third and final dose of Hepatitis B vaccine – three doses are recommended for full protection.</td>
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<tr>
<td><strong>Perinatal transmission</strong></td>
<td>Transmission from mother to child at the time of birth.</td>
</tr>
<tr>
<td><strong>Plasma-derived hepatitis vaccine</strong></td>
<td>Hepatitis B vaccine manufactured from the plasma of HbsAg+ carriers by extracting the HBsAg.</td>
</tr>
<tr>
<td><strong>Recombinant hepatitis vaccine</strong></td>
<td>Hepatitis B vaccine manufactured from a genetically modified yeast cell or from a mammalian cell with the gene to produce HBsAg.</td>
</tr>
<tr>
<td><strong>Seroprevalence</strong></td>
<td>Percentage of a population whose sera are positive for a specific marker such as an antibody (e.g. antiHBs or antiHbc) or an antigen (e.g. HBsAg or HBeAg).</td>
</tr>
<tr>
<td><strong>TBA</strong></td>
<td>Traditional birth attendant</td>
</tr>
<tr>
<td><strong>Uniject</strong></td>
<td>A single use, plastic disposable syringe attached with a permanent needle and prefilled with a single dose of medicament.</td>
</tr>
<tr>
<td><strong>VVM</strong></td>
<td>Vaccine vial monitor – a heat sensitive indicator attached to a vaccine vial to monitor the exposure of the vaccine to high temperatures.</td>
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Who should use this manual?

- National or subnational immunization and maternal health programme managers and policy-makers.

How can this guide assist national immunization programmes?

- By providing a menu of programmatic options for improving timely delivery of the first dose of hepatitis B vaccine in different birth contexts to reduce mother-to-child transmission of the disease.

- By providing best practice examples from a variety of countries applicable to a variety of contexts, especially with respect to place of birth.

When do you need this guide?

- When deciding on programmatic strategies for delivering the timely birth dose of hepatitis B vaccine in different birth contexts.

How can you use this guide?

- As an operational manual to plan, implement and monitor the delivery of the timely birth dose of hepatitis B vaccine.
1. Introduction

How Important is Prevention of Mother-to-Child Transmission to Hepatitis B Control Goals?

- In the Western Pacific Region, mother-to-child transmission and early childhood exposure are the most important mechanisms of hepatitis B transmission. In most countries in the Region, up to 50% of children\(^1\) may become infected during the first five years of life if they are not vaccinated. (Please see Box 1 for a discussion on modes of transmission of hepatitis B, and Box 2 for a discussion on how the virus is transmitted from mother to child.)

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**Box 1: How is the hepatitis B virus transmitted from one person to another?**

- Percutaneous or mucous membrane contact with infected blood or other body fluids (e.g. serous exudates from a wound or cut, saliva, semen or vaginal fluids).
- HBV is not transmitted by air, food or water.
- As there is no animal reservoir for the virus, the virus cannot be transmitted by animals.

**The primary routes of HBV transmission are:**

- Mother-to-child transmission during birth.
- Transmission between children through cuts, scrapes, bites and scratches (early childhood transmission).
- Sexual contact.
- Unsafe injections and blood transfusions.

- About 10% of mothers in the Region, most of whom may be unaware of their infection status, are chronic HBV carriers at risk of transmitting HBV infection to their newborn babies at birth.

- From the public health perspective, preventing infections acquired at birth and in early childhood is critical, as children have a 90% chance of becoming chronic carriers if infected at the time of birth, a 30% chance of becoming chronic carriers if infected between one and five years of age, and a 5% to 10% chance of becoming chronic carriers if infected after five years of age.

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\(^1\) Although not all infected children will become chronic carriers or develop acute hepatitis.
Box 3: What is the key programmatic strategy for hepatitis B control?

Safe injection practices and promotion of safe sex can play an important role in preventing infection in all age groups and should be pursued as goals in their own right, but universal infant immunization is considered to be the most effective strategy to control hepatitis B. In most countries, including countries with low prevalence rates of chronic infection, a disproportionate number of persons with chronic hepatitis B infection acquire their infection in early childhood, when the risk is highest. Therefore, vaccination in the first year of life is the key recommended strategy.

- Three doses of hepatitis B vaccine given at intervals of at least one month are 95% effective in preventing future infection.

Box 2: How is the hepatitis B virus transmitted from mother to child?

- Transmission from infected mothers to their infants takes place primarily at the time of birth. A newborn infant has a 10% to 90% chance of becoming infected at the time of delivery if its mother has chronic hepatitis B infection. The probability of transmission increases substantially if the mother is positive for both HBsAg and HBeAg, indicating active viral replication. It is estimated that 20% to 40% of HBsAg-positive mothers may be positive for HBeAg as well.

- Evidence suggest that in utero transmission is relatively rare, accounting for less than 2% of all infections transmitted from mother to infant. Instead, transmission occurs during the birth process, when contact with blood always occurs.

- There is no clear evidence that the hepatitis B virus is transmitted by breast-feeding.

- There is no clear evidence that alternative birth techniques, such as caesarean section, will prevent or reduce the risk of transmission.

• Every chronic carrier of hepatitis B will act as a source of infection for the rest of his/her life. Hence, infected children will continue to sustain the reservoir of infection for HBV transmission to other children and will be at risk for chronic liver disease and liver-disease-related death in adulthood.

• Despite other interventions to control hepatitis B, in the absence of measures to prevent mother-to-child transmission, an estimated 3% to 5% of all infants born in the Region will acquire chronic hepatitis B infection at birth.

• For every year that the birth dose is delayed, the elimination of hepatitis B from the Region will be compromised, and many deaths due to cirrhosis and cancer of the liver will occur among future generations.
How can Mother-to-Child Transmission be Prevented?

- Hepatitis B vaccine is effective in preventing infection after a person is exposed to the virus (by any means), if given soon enough after exposure. Hence, if the first dose of hepatitis B vaccine is given as soon as possible after birth (within 24 hours), hepatitis B infection can be prevented in a newborn infant.

- In addition to the hepatitis B vaccine, HBIG (hepatitis B immunoglobulin) can be given as an intramuscular injection to babies born to mothers known to be positive for HBsAg. While some studies have documented additional protection conferred by HBIG, other studies have indicated limited additional protection, over and above that provided by hepatitis B vaccine. However on operational and cost-effectiveness grounds, universal use of HBIG is not necessary, especially in countries where pregnant women are not screened for HBsAg.

Preventing mother-to-child transmission — Don’ts:

- Do not vaccinate the mother ‘known to be chronic carrier of hepatitis B’ during pregnancy! Doing so is neither advisable nor effective in preventing the transmission of infection from already chronically infected mothers to their newborn infants.
Box 4: How does the rationale and importance of giving the first dose of hepatitis B differ from that of other vaccines (e.g. BCG) recommended at birth?

The main reason to give the first dose of hepatitis B vaccine immediately after birth is to prevent establishment of the infection to which the newborn infant is already exposed. The birth dose is a post-exposure prophylaxis. Other vaccines recommended at birth, such as BCG and OPV, are given to prevent future infection. Thus, for hepatitis B vaccine it is imperative to shorten the interval between birth and the administration of the first dose.

How Effective is the Vaccine in Preventing Mother-to-Child Transmission?

- The protective efficacy of the hepatitis B vaccine in preventing mother-to-child transmission ranges from 80% to 95%.

- The efficacy of the vaccine in preventing perinatal transmission declines with increasing intervals between birth and the administration of the vaccine. It is therefore recommended that the first dose of hepatitis B vaccine be given within 24 hours of birth.

Box 5: What if sustained high coverage with three doses of hepatitis B vaccine is maintained, with first dose of the vaccine given along with first dose of DTP, (generally at six weeks to two months of age)?

Three doses of hepatitis B vaccine — if started late — at six weeks to two months of age, will not prevent perinatal transmission.

Despite sustained high coverage with three doses of hepatitis B vaccine, without the birth dose, an estimated 3% to 5% of all infants born in the Region will acquire chronic hepatitis B infection at birth, way above the target (less than 2% by 2012 and <1% in the future) set for hepatitis B control.
The following sections provide operational programmatic guidelines for provision of the birth dose of hepatitis B vaccine. The guidelines assume that the country has a programme for universal infant immunization with hepatitis B vaccine, including an official policy for delivery of the first dose within 24 hours of birth.

**Figure 1.** This 40-year-old man in Mongolia is spending his productive years in a hospital due to chronic liver disease which can now be prevented with hepatitis B vaccine.

The Western Pacific Regional goal for hepatitis B control

Reduce the chronic infection rate to less than 2% among five-year-olds by 2012, as an interim milestone to the final goal of less than 1%.

The keys to achieving this regional goal are reducing mother-to-child transmission by timely birth dose and sustained high coverage with three doses of hepatitis B vaccine.
2. Delivering the Birth Dose Within 24 Hours: The Challenges

Improving Access to Trained Maternity Care

Despite special efforts being made in the last decade to improve women’s access to trained maternity care, a significant proportion of births in many developing countries in the Region continue to take place at home, with limited access to trained maternity care providers (see Annex 1). Access to a trained provider competent to give an injection to a newborn infant at the time of birth is a prerequisite to administering the birth dose of hepatitis B vaccine. Lack of such access may constrain the increase in coverage of the timely birth dose.

Ensuring the Availability of the Vaccine at the Time of Birth

The birth dose is delivered at a different location from other EPI vaccines.

The vaccine needs to be made available as near to the place and time where and when mothers give birth. However, other vaccines (except BCG) and subsequent doses of hepatitis B vaccine are usually delivered in a different location from the birth site, such as in well-baby clinics or in outpatient health clinics, or during outreach immunization sessions in the community.

The two key challenges in the delivery of the birth dose are:

- Ensuring access to a trained service provider at the time of birth
- Ensuring access to the vaccine at the time of birth
The birth dose cannot be delivered using an ‘immunization day’ or immunization session approach.

Timely delivery of the birth dose requires access to hepatitis B vaccine 24 hours a day every day, as births take place all the time.

**The birth dose may need to be delivered outside the cold chain.**

A substantial proportion of births in developing countries take place either at home or in lower-level health facilities that lack a continuous cold chain. Such facilities tend to collect vaccines from the higher-level facilities at periodic intervals (generally once every 1-3 months) in a vaccine carrier/cold box and store the vaccines at the health facility for two to three days only. Hence, such facilities remain without any vaccine for substantial periods of time and are unable to provide a birth dose for all births.

**Special guidelines need to be developed for storage and distribution of hepatitis B vaccine, specifically for the birth dose, in order to make it available as and when birth occurs.**

**Involving the Maternity Staff in Addition to EPI Staff**

Generally, a nurse, paediatrician or general physician delivers immunization services. However, the birth dose may have to be given by an obstetrician, obstetric or neonatal nurse, or a midwife attending the birth. Hence, **all maternity staff** need to be made aware of the need for immunization to prevent hepatitis B and be trained to provide the injection.

**Figure 2.** Maternity staff must be involved and trained to provide the vaccine immediately after birth.
Recording the Birth Dose

In countries with manual recording systems, immunization registers and child immunization cards are generally kept in well-baby clinics or at the place where other immunizations are delivered. A separate recording and reporting system may need to be developed for the first dose of hepatitis B vaccine to enable recording of the dose administered in the maternity room/ward.

Safety of the Birth Dose

Vaccine is administered at a time when infants are most vulnerable to co-incidental adverse effects. The first day of life is a high-risk time for neonatal deaths and this may lead to rumours of deaths linked to vaccines. Special pre-emptive communication efforts will therefore be needed to assure parents of the importance and safety of timely hepatitis B vaccination at birth.

Box 6: Delivery of the birth dose needs closer collaboration between national immunization systems and maternal health services.

The hepatitis B vaccine birth dose cannot be delivered efficiently under a vertically structured national immunization programme. In vertically structured programmes, maternity staff are typically not included in any immunization-related training programmes and may not even be aware of hepatitis B, its transmission at birth, or the need to provide an injection within 24 hours of birth.

**In a scenario in which there is no other trained provider at the time of birth except maternity staff,** an indispensable prerequisite will be the collaboration of EPI staff with the maternal health staff who provide antenatal, maternity and postnatal care. Thus the maternal health staff need to be:

- included in training programmes to help them to provide information on the hepatitis B birth dose to their antenatal care clients;
- trained to administer the injection after birth and record the information in a parent/child-held immunization card; and
- trained to inform the EPI staff about hepatitis B vaccination in circumstances in which the maternity staff are not able to provide the service.
3. Opportunities for Early Administration of Hepatitis B Vaccine

High Priority Given to Increasing Access to Trained Delivery Care

Increasing access to trained delivery care for at least 90% of all deliveries, preferably in institutional settings, is an important Millennium Development Goal, set by the United Nations and endorsed by all Member States. Since access to trained delivery care is a prerequisite for timely administration of the hepatitis B vaccine birth dose, there is an opportunity for synergy between EPI and maternal health programmes. Focusing on timely birth dose delivery will provide an impetus for early contact between the mother, the newborn infant and the health worker, with the attendant multiple health care benefits of such contact. Coverage of hepatitis B birth dose may also be used as an indicator to monitor the coverage of trained delivery care.

In addition, delivery of the birth dose fits easily into the strategy for integrated management of childhood illnesses (IMCI), which incorporates essential postnatal care of all neonates through home contact within 24 hours of birth, as well as appropriate disease prevention and treatment strategies.

Figure 3. Increasing access to trained delivery care is a Millennium Development Goal and a high public health priority in the majority of Member States.

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2 Millennium Development Goal 5 aims to improve maternal health by reducing the maternal mortality ratio by three-quarters by 2015. Access to trained delivery care is an indicator to monitor the achievement of the goal. The objective is to ensure access to trained delivery care for at least 90% of births by 2015.
Vaccination or Injection Immediately After Birth is not a New Strategy

Administering vitamin K injections to newborn infants immediately after delivery is standard practice in many countries. Administering BCG vaccine is universally recommended as soon after birth as possible. In addition, many countries recommend that maternity care include an oxytocin injection for the mother in the third stage of labour to reduce bleeding. These recommendations already require providers to be trained in injection techniques. The provision of hepatitis B vaccine after birth can easily be built upon these measures.

Relative Heat Stability of Hepatitis B Vaccine

As demonstrated both in laboratory testing and in seroconversion rate comparison among different groups given the vaccine stored under varying temperature conditions in actual service delivery settings, hepatitis B vaccine is relatively heat stable. The hepatitis B vaccine vial, along with the attached vaccine vial monitor (VVM), can be stored out of the cold chain (OCC) for extended periods in situations lacking a continuous cold chain. See Annex 3 for further details.

Combining the Birth Dose with Other Postnatal and Neonatal Care Interventions

Early contact between the health worker and the mother and infant is a cost-effective way to bring a wide range of public health benefits to communities lacking quality routine health care services.

Possible postnatal and neonatal care interventions immediately after birth may include a postnatal check-up and vitamin A and iron supplementation for the mother, and other vaccinations (BCG) for the newborn infant. In addition, they give an opportunity for health workers to provide health education on cord care and other aspects of newborn care, including exclusive early breast-feeding, identification and special care of low-birth-weight babies, and maternal care.
Earliest Protection Against Horizontal Hepatitis B Transmission

An early birth dose, not only prevents mother-to-child transmission of hepatitis B infection, but also provides the earliest possible protection against horizontal transmission from infected family members, other children and caregivers.

Potential to Increase Coverage for Subsequent Doses of Hepatitis B Vaccine and Other Vaccines

Administration of a vaccine at birth provides the earliest possible opportunity to give information to new parents on childhood immunization. Delivery of the birth dose, accompanied by appropriate health education and provision of a newborn infant immunization record, has the potential to sensitize parents to the need for subsequent doses of hepatitis B vaccine and other vaccines, and may greatly increase the likelihood of a child completing the vaccination schedule.

Administration of the Birth Dose is an Equity Issue

Access to trained delivery care shows the most iniquitous distribution by socioeconomic status of all health care outputs or outcome indicators. Providing the birth dose to all infants will require more pro-active and aggressive strategies to reach underserved populations with trained delivery care.
4. Operational Guidelines and Strategies

Field guidelines and strategies to deliver and increase birth dose coverage will vary greatly in different contexts and situations depending upon:

- the **place** of maternity care;
- the **provider** of maternity care; and
- the **organization, relationship and coordination** between EPI and the maternal service staff.

To ensure that customized programmatic strategies are developed to ensure that all newborn infants, irrespective of the place or provider of services, are able to receive the timely birth dose, births are categorized into four major groups, based on the birth context:

- **Births in public health facilities** with access to a continuous cold chain;
- **Births in private health facilities** with access to a continuous cold chain;
- **Births in lower-level health facilities** without access to a continuous cold chain; or
- **Births at home**:
  - assisted by a trained provider competent to provide injections; or
  - assisted by a birth attendant not competent to provide injections.

To ensure equity in access, it is necessary for programme managers to monitor timely birth dose coverage for each birthing context (i.e. home births, hospital births, etc.) separately.

Before describing specific programmatic strategies applicable to each birthing context, the next section describes the common operational strategies applicable to all births.

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**All efforts should be made to increase access to institutional, trained maternity care, in line with the Millennium Development Goals.**

**Customized programmatic strategies need to be developed in the interim to make sure that all newborn infants, irrespective of place or provider of birth services, are reached.**
1. **Undertake a situation analysis of maternal and neonatal health services.**

As a first step, EPI managers should meet with maternal and child health staff and visit a few maternity facilities to carry out a situation analysis to answer the following questions:

- Where are births taking place? What proportion of births take place in different levels of public sector health facility, in private health facilities or at home?
- Who is providing maternity care in each setting and what are the competencies of the staff providing such care?
- What other maternal and neonatal care interventions are provided within 24 hours of birth (e.g. vitamin K injection to newborn babies or oxytocin injection to mothers)?
- How are the other vaccinations recommended at birth (e.g. BCG) being provided?
- What efforts are being made to increase births in hospital or to ensure trained attendants are present at births?

2. **Conduct joint planning with maternal health services staff.**

Immunization services managers should work with maternal health services staff to develop plans clearly specifying the following for each birth context:

- Where the birth dose should be provided (labour room, vaccination room, post-delivery obstetric ward, home, health centre, etc.).
- Who should give the birth dose.
- How to ensure vaccine availability and its proper storage.
- How to record the birth dose.
- How to inform parents about the birth dose.

3. **Proceed from easy to difficult — from institutional births to home births.**

Programmatic strategies to increase the timely birth dose may be much easier to develop, implement and monitor for institutional births than for home births because of institutional access both to trained providers and to vaccines at the time of birth.
If special efforts needing substantial additional resources are required to reach home births, first ensure that 100% of institutional births are covered while continuing efforts for home-based births.

**Box 7: Expanding birth dose coverage: proceed from easy to difficult!**

Discussion about expanding coverage of the hepatitis B vaccine birth dose automatically raises issues concerning home deliveries and lower-level health facility deliveries, but delivery of the timely birth dose in institutional births remains an unacknowledged problem.

Recent reviews in the Western Pacific Region show that coverage with a timely birth dose may be low even among those births taking place in tertiary hospitals, despite the availability of both the vaccine and the trained personnel to provide the injection. Reasons for low coverage range from low awareness among maternity staff, to false contraindications, lack of coordination between EPI and maternity staff, and sometimes, simply incorrect programmatic strategies.

**EPI managers should not assume that all institutional births will automatically receive a timely birth dose.** Specific programmatic strategies, as described later, will need to be developed and implemented to ensure delivery of a timely birth dose, even for births taking place in health facilities. It is just as important to monitor birth dose delivery in institutional settings as in home-based settings.

4. **Train maternity and paediatric staff.**

Who to train and what to train them in will depend on the staff who are present at the time of birth and their decision-making powers (i.e. who makes the decision about what interventions are to be given to newborn infants — the attending physician, midwife, neonatal nurse, etc.) Maternal services staff will require training on hepatitis B, its transmission and the importance of early hepatitis B vaccination, so that they can inform mothers of their infants’ needs during the antenatal period and can provide the vaccine when they are the only attending staff. Training may also be required for attending physicians/paediatricians if they are the main decision-makers for neonatal interventions, to avoid denial of the vaccine because of incorrect contraindications. Please see Box 9 on page 16 for a checklist of topics to be included in the training.

5. **Change antenatal care protocols/guidelines.**

In most countries, the antenatal care guidelines specify the need to inform mothers during their third trimester visits about the immunization needs of their children. The guidelines should be modified to include information on the need for a hepatitis B vaccine
injection for newborn infants within 24 hours of birth. Accordingly, all staff involved in providing antenatal care should be trained in informing mothers about the importance and need for early hepatitis B vaccination. The mother should also be asked where she plans to deliver so that the vaccine can be made available at the place of birth. Such information will create demand from parents for the hepatitis B vaccine birth dose for their newborn infants.

Box 8: Delays in administering the hepatitis B vaccine birth dose may occur even in health facilities: a review of practices in Cambodia, the Lao People’s Democratic Republic and Mongolia.

Cambodia: Vaccinations in Cambodia are provided only in the lowest-level health facilities. Although there are staff who are competent to give injections at the time of birth, they are not involved in providing vaccines in hospitals or in higher-level health facilities. All mothers giving birth in higher-level facilities are asked to take their newborn infants to the nearest health centre for the birth dose. There is no follow-up by hospital staff to determine whether or not children receive the vaccine.

The Lao People’s Democratic Republic: The hepatitis B vaccine birth dose was first introduced on a pilot basis in four hospitals in 2004. In one hospital, mothers were asked to take their newborn infants to the vaccination room for their hepatitis B vaccine birth dose, where a special, dedicated nurse provided vaccinations. However, services were provided only from 9:00 am to 5:00 pm, Monday to Friday. The system resulted in low coverage for all newborn babies, especially for births taking place on Saturdays and Sundays. In another hospital, the attending physician provided the injection in the delivery room, with the vaccine being stored in a vaccine carrier in the same room. The second approach resulted in almost 100% coverage.

Mongolia: All newborn infants are given a vitamin K injection by a neonatal nurse in the labour room within two hours of delivery. Mothers are sent to a postpartum ward within two to three hours of delivery. In the postpartum ward, a separate ‘vaccinator’ nurse is responsible for administering the hepatitis B vaccine birth dose, along with BCG and a birth dose of OPV, on the basis of recommendations made by the attending paediatrician, and as noted on the newborn-infant care sheet. Since the vaccinator nurse is not aware of the importance and purpose of the hepatitis B birth dose, she administers the vaccine at her own pace before the mother is discharged from the hospital, which may be two to three days after the birth.
6. Include hepatitis B injection in the essential care package for newborn infants and make necessary changes in the newborn-infant care protocol.

Provision of hepatitis B vaccine as early as possible after birth — preferably within 12-24 hours — should be added as an essential component of the newborn-infant care protocol.

7. Record and report the birth dose.

Appropriate recording and reporting of the birth dose may require modification of child immunization records and/or development of special forms for recording and reporting the birth dose to mothers and future immunization providers.

- Modify parent/child-held immunization records. The format of immunization records should be modified with provision of a special column for entering the date and time of the hepatitis B vaccine birth dose (see Figures 5 and 6).
- If a child immunization card is not issued at birth, forms must be developed to record and track the birth dose at the hospital, and to give to parents to inform future immunization providers. For example, China has developed a triplicate record for this purpose, with copies provided both to parents and to future local immunization providers, according to the infant’s residence.
8. Ensure monitoring of the birth dose coverage by the national immunization programme/EPI.

As the old adage goes, “what gets monitored gets done,” so timely birth dose coverage must be monitored at all administrative levels (i.e., district/provincial/national) and appropriate programmatic action taken where coverage is below expected levels. In addition, birth dose coverage should be monitored by birthing context, e.g. coverage for institutional births and coverage for home births. As mentioned earlier, birth dose coverage can also be used as an alternative indicator for access to trained delivery care.

9. Inform, educate and communicate with health care providers in both the public and private sectors, as well as with parents.

Special messages need to be developed targeting providers as well as parents, making both groups aware of the need for the birth dose.
Vaccine Formulations, Vial Presentations and Storage

1. Choosing the vaccine formulation for the birth dose.

Only monovalent vaccine is suitable for the birth dose. Combination vaccine (e.g. DTP-HepB or DTP-Hib-HepB) cannot be used for this purpose.

In countries using combination tetravalent or pentavalent hepatitis-B-containing vaccine:

- The birth dose of monovalent hepatitis B vaccine will be used in addition to the three doses of combination vaccine needed to complete the vaccination schedule.

2. Choosing the vaccine vial presentation for the birth dose.

Monovalent hepatitis B vaccine is available in several vial presentations:

- single-dose vials — traditional vial bundled with standard AD syringe or UNIJECT device;
- two-dose vials;
- six-dose vials; and
- ten-dose vials.

The suitable vaccine vial formulation needs to be chosen based on the primary context in which births take place and the trade-off involved between vaccine wastage, costs and the additional cold chain space required. The weighted average price per dose in different presentations, as published by UNICEF in 2005, was US$0.41 (one-dose vial); US$0.36 (two-dose vial); US$0.623 (six-dose vial); and US$0.27 (ten-dose vial).
If the majority of births take place in large institutional settings with a continuous cold chain (where a multi-dose vial policy would be applicable), with at least one to two births taking place daily, then multi-dose vials — either six-dose or ten-dose3— may suffice.

If the majority of births take place in lower-level health facilities with no continuous cold chain (and thus multi-dose vial policy [MDVP] will not apply) or at home, one-dose or two-dose vials may be the best choice to reduce vaccine wastage.

In countries with a mixture of hospital births and home births, a fraction of the total hepatitis B vaccine may be ordered as single-dose vials, with the remainder ordered in the usual two-dose, six-dose or 10-dose vials.

**Using Hepatitis B Vaccine Where Continuous Cold Chain Cannot be Maintained.**

Hepatitis B vaccine has proven to be remarkably heat stable, both in laboratory testing and in actual field conditions, as demonstrated by studies conducted in China, Indonesia and Viet Nam. (See Annex 3 for more details on these studies.) Hepatitis B vaccine can be stored safely at ambient temperatures for up to one month without significant loss of potency. Thus the hepatitis B vaccine for the birth dose may be stored and used out of the cold chain (at ambient temperature) at point of use whenever the regular cold chain cannot be maintained (e.g. in the lowest-level health facility or by a midwife for home births).

Hepatitis B vaccine for OCC use may be available either in vials, as single-dose or multi-dose formulations, or as UNIJECT devices (single-dose). **Programme officers should ensure that national regulatory authorities have approved the use of hepatitis B vaccine out of the cold chain.**

**Detailed instructions for storing hepatitis B vaccine out of the cold chain are provided below.**

**The following conditions need to be met to store the vaccine out of the cold chain:**

1. The vaccine must have been stored appropriately in the cold chain at all other points of storage/distribution before reaching the lowest point of use.
2. The VVM must be attached to the vaccine vial to monitor any heat damage.
3. The attached VVM must not have reached its discard point.
4. The vaccine vial must not be past its expiry date.
5. The vaccine must not show any signs of past or current freezing4 (passes the shake test).

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3 Although the price per dose for the six-dose vial is currently higher than for one-dose or two-dose vials, as there is only one manufacturer for this vial formulation.

4 This concern is especially important in countries, such as Mongolia and in northern China, that experience sub-freezing temperatures for significant periods of time.
(1) Vaccine vials out of the cold chain must be stored in a location protected from direct sunlight, extreme heat and cold (freezing), and tampering.

(2) The current MDVP does not apply to storing opened vials of hepatitis B vaccine out of the cold chain. All remaining doses in an opened multi-dose vial in an OCC setting should be discarded within six hours to make it consistent for other opened lyophilized vaccines (e.g. measles).

Vaccine Vail Monitor (VVM) on hepatitis B vaccine vial/ampoule/unject will be a precondition to use of vaccine outside cold chain.

**Storage out of the cold chain is not applicable for:**

- vaccine at national/provincial, district or other levels where a continuous cold chain facility is available (Even at the lowest level, vaccine should be kept within the cold chain at 2°-8°Celsius to the extent possible);
- open multi-dose vials; or
- subsequent doses of the primary series. As far as possible, use of hepatitis B vaccine out of the cold chain should be limited to only the birth dose, while the hepatitis vaccine for subsequent doses (2nd and 3rd dose) and other vaccines should be stored according to cold chain guidelines.

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5 Please note that for MDVP to apply, the opened vaccine vials must be stored between 2° and 8°Celsius. Thus, assuming that OCC policy will be used only when refrigeration is unavailable, this condition of MDVP will not be fulfilled.
**Duration of out of cold chain storage:**

Technically, hepatitis B vaccine can be stored OCC as long the VVM is not past its discard point, but most of the existing studies that have tested the effectiveness of hepatitis B vaccine stored OCC under service delivery conditions have tested it for one month or less. Thus, until more studies demonstrate the effectiveness of OCC hepatitis B vaccine beyond one month, it is currently recommended that hepatitis B vaccine OCC be used for one month only. Hence, at point of use, the vaccine may be stored for a maximum of one month outside the cold chain. After one month, any remaining vaccine must be discarded. The one month measure applies to the total duration of storage outside of the cold chain. For example, if the vaccine is stored out of the cold chain at the lowest-level health facility and is then taken to the midwife’s home, the total duration of out of cold chain storage (time in the health facility plus time in the midwife’s home) should not exceed one month. The vaccine needs to be discarded even when it is stored for less than one month outside cold chain if it is past its expiry date, if the attached VVM indicates heat damage, or if there is evidence of vaccine freezing (in countries such as Mongolia where the outside temperature may be below freezing point).

The health worker should write on the vial the date, one month after removing from the cold chain, indicating that the vaccine cannot be stored outside after that date and needs to be discarded. These instructions are similar to the instructions for using vaccines under ‘multi-dose vial policy’, in which vaccines can be used only up to 28 days after opening the vial.

Programmatically, one month should serve most community purposes, since the lowest point of use usually collects vaccines from higher levels each month. Further, vaccine storage boxes are small, and excessive amounts of hepatitis B vaccine may crowd other vaccines.

\[
\text{Time OCC in the health facility} + \text{time OCC at the midwife’s home} \leq \text{one month.}
\]
Specific Guidelines — Depending on the Place of Birth and the Vaccine Provider

Group A. Births in public sector health facilities with access to a continuous cold chain:

In many countries in the Region, such as Brunei Darussalam, Malaysia, Mongolia, New Zealand, the Republic of Korea, Singapore and most of the Pacific island countries and areas, the majority of births take place in public sector health facilities with a continuous cold chain. In addition, in countries such as China, the Philippines and Viet Nam, a substantial number of births occur in public health facilities.

In such settings, the specific programmatic approaches that may be required in addition to the approaches underlined in the previous section include:

1. Assign responsibility for providing the birth dose.

This step is necessary to ensure that there is no confusion about who (obstetrician, paediatrician, EPI nurse, etc.) will provide the birth dose. A system should be in place to ensure that there is a designated person 24 hours per day, seven days per week, to provide the timely birth dose in the health facility.

2. Make the vaccine available. Work out the logistics of vaccine supply and management.

The logistics should be worked out to ensure that the vaccine is available where needed, in the maternity room/ward (see Figure 7). Each hospital with a maternity room/ward may be requested to submit to national/provincial/district immunization managers a monthly request for vaccine based on the average number of births each month. Upon receipt of the vaccine, the hospital will be responsible for ensuring that it is available in the maternity room/ward.

The vaccine may be stored directly in the maternity room/ward if a dedicated refrigerator is available. Or it may be stored in a common refrigerator in the hospital, and daily needs may be taken out and kept in a vaccine carrier in the maternity room/ward.
3. Record and report.

Since subsequent immunization for the child will, in most cases, be given by a different provider in a different place, it is important to give a record to the parents of the child of the immunization administered at the time of the birth. This record will enable subsequent providers to know what immunizations were given to the child at the time of birth.

Different options for providing this record might be:

- **Parent/child-held immunization cards may be provided in the maternity room itself.** Before the birth dose for hepatitis B was introduced (despite the recommendation for a birth dose of BCG), vaccinators generally issued cards when a child was brought in for the first vaccination (generally for DPT1). However, to ensure that maternity staff record birth doses of hepatitis B, those cards now need to be made available in the maternity room/ward.
• A separate, special record may be developed for this purpose, which may be
taken by the mother to the subsequent provider. The regular provider will enter
the birth dose in the child immunization card later. This practice is followed in China
and in Viet Nam.

• A separate birth dose registry may be held at the health facility, if possible in
duplicate. The registry will help to monitor success in achieving timely birth doses at
the hospital. In addition, a monthly report listing each child may be sent to the EPI
health worker, who can then add those children to the immunization register at the
health facility and follow up on the children for the rest of their immunizations.

**Box 10. Checklist for births in public sector health facilities with continuous access
to cold chain:**

- Put logistics in place to supply and store the vaccine in the maternity ward/room.
- Identify a clearly designated staff member who will be responsible for administering the vaccine and ensuring that a designated staff member is present all the 24 hours each day.
- Have recording and reporting forms, with columns to record birth doses, available in the maternity room.
- Train the maternity services staff.
- Modify the newborn infant care protocol

**Box 11. Common practices that need to be discouraged in hospital/health facilities.**

- Discourage the tendency among health providers to give the vaccine at the time of the mother’s discharge from the health facility. Instead, give the birth dose as soon as possible after birth.
- Discourage advising the mother to take the baby to the nearest primary health care facility or to the vaccination unit in the hospital for the birth dose. Instead, provide the vaccination in the place of birth. Mothers may never take the child to the primary care health facility, resulting in a missed opportunity to provide a timely hepatitis B birth dose to the newborn infant.
- Discourage false contraindications (low birth weight, prematurity) to delay administration of the birth dose.
Group B. Births in private sector health facilities with access to a continuous cold chain

A substantial proportion of births in China, Malaysia, the Republic of Korea and Viet Nam take place in private sector maternity homes that may have refrigerators for storing the vaccine at an appropriate temperature.

The programmatic strategies for ensuring timely delivery of birth doses in private sector health facilities are similar to strategies for involving the private sector in the provision of immunization services in general. Although the private sector plays an important role in many countries in providing public health services, it is typically not included in the training programmes and may not be viewed by the public sector as an important partner in the provision of immunization services. However, the increasingly important role and demand for private sector health care warrants proactive efforts by national immunization programmes for the inclusion of the private sector in providing immunization services—including attending training programmes and monitoring the services the sector provides.

All procedures recommended for public facilities also apply to private facilities. The following additional areas may require special emphasis

1. Ensure private sector involvement in hepatitis B vaccination programme by taking the following steps:

- Contact the obstetrician/paediatrician associations in your country.
- Contact and involve any private sector provider associations.
- Write letters to private sector maternity homes to introduce, and then to continue the practice of administering the birth dose within 24 hours of birth.
- Supply free communication materials to private maternity homes.
- Increase awareness among prospective parents about the need for the timely birth dose. Doing so will increase demand from parents, who may request the hepatitis B vaccine. Broadcast advertisements on television and radio in order to reach the population utilizing private sector health care.
2. **Ensure the availability of vaccine in private clinics and hospitals.**

Ensure the availability of quality vaccines in private facilities, even when it means **supplying the vaccine free of charge in return for the provision of services.** Private health facilities willing to participate in the programme should be requested to submit monthly/quarterly demands for vaccine. Based on each situation, the National Immunization Programme may supply vaccines either free, subsidized or at full cost.

3. **Ensure the quality of the timely birth dose delivered in private health facilities.**

- Ensure that private providers have training on the safe provision of immunizations.
- Ensure that private facilities have an adequate cold chain, safe vaccine storage and vaccine temperature monitoring.
- Ensure the utilization of safe injection techniques.
- Ensure monitoring systems are in place for the timely birth dose.

4. **Develop systems in the national immunization programme to monitor the delivery of vaccines in private maternity homes.**

Put in place incentive systems in return for private sector accountability to the national immunization programme. Provide, for example, free vaccine supply to private sector institutions that demonstrate in an ongoing fashion that their vaccine is being stored in an appropriate manner, and that routine services are being provided and reported to the EPI manager.

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**Figure 8. Involving private sector may be important to expand coverage with hepatitis B birth dose.**
Group C. Births in lower-level health facilities with no continuous cold chain

In countries such as Cambodia, China, Papua New Guinea, the Philippines and Viet Nam, a substantial proportion of births may take place in health facilities lacking access to a continuous cold chain. Most such health facilities provide immunization services in their catchment areas using the immunization day/session approach. Such immunization sessions may be held on one or two days a month, or every two to three months. The health facilities normally collect vaccines in a vaccine carrier or in a cold box, and only at the time of the immunization session, based on estimated demand for one session only. The absence of cold chain equipment creates periods without vaccine availability, because according to the current recommendations, hepatitis B vaccine, as well as other vaccines, can only be kept at the current recommended storage temperature (2°-8° Celsius) in the vaccine carriers/cold box for two to three days. Thus, one of the major challenges will be to ensure continuous vaccine availability to these health facilities so that the vaccine can be administered when a birth takes place.

1. Make the vaccine available on a continuous basis: implement guidelines for the use of vaccine OCC in lower-level health facilities.

Programme managers need to develop detailed implementation guidelines for health workers on the use of vaccine out of the cold chain, as outlined earlier. The OCC can be implemented on an initial pilot basis or rolled-out nationally in a phased manner. The implementation of OCC should be carefully monitored, at least in the initial years of implementation.

Different formulations of hepatitis B vaccine (such as single-dose vaccine or Uniject) may be obtained for the birth dose than for the subsequent doses in order to differentiate the vaccine to be used for the birth dose and retained OCC.

2. Provide special training for midwives/vaccinators in lower-level health facilities.

The staff in the lower-level health facility who will be using the vaccine out of the cold chain should be adequately trained in handling, storing and transporting the vaccine. This training will be in addition to the list of topics provided in the training checklist in Box 9.

3. Other operational elements.

Other operational elements may include modifying the newborn infant care protocol; making special arrangements for recording and reporting the administered birth dose, including making available child-held immunization cards; and creating a demand among parents for an early dose of hepatitis B vaccine, as outlined earlier.
Group D. Births taking place at home

A significant proportion of births in countries such as Cambodia, China, the Lao People’s Democratic Republic, Papua New Guinea, the Philippines and Viet Nam take place at home (see Annex 1).

Such a situation is the most challenging, requiring proactive efforts to increase the reach of trained delivery care. At-home births may also necessitate taking the vaccine out of the cold chain. Areas with a high prevalence of home deliveries are generally areas where immunization services are provided through outreach, or where the health facilities responsible for immunization do not have a continuous cold chain.

At-home births can be divided into two categories: births attended by trained health workers competent to give injections, and births attended by untrained attendants (such as traditional birth attendants or family members).

At-home births with trained attendants competent to give injections:

1. Make the vaccine available to midwives.

This procedure will, in most instances, require storing the vaccine out of the cold chain either at the lower-level health facility or at the home of the midwife, according to the instructions outlined earlier.

(a) Change the midwives’ kits for home delivery:

- Make hepatitis monovalent single-dose vials bundled with AD syringes an integral part of the midwifery kit.

(b) Four different ways to deliver the vaccine in home-based births attended by a trained health worker:

- The midwife may collect the vaccine, along with her midwifery kit, at the expected time of delivery from the lower-level health facility, where it might be stored within or out of the cold chain, and store it appropriately at her home until the birth. This system is feasible if the midwife is a staff member of the health facility and collects her midwifery kit regularly from the health facility at the time of a birth or just before a birth.
• Midwives may collect monthly vaccine supplies, based on the expected number of births they are going to assist, and then store the supplies at their homes out of the cold chain. Midwives may collect vaccines from the nearest health facility that keeps vaccines on a continuous basis within the cold chain. Or midwives may collect vaccines from the lower-level facility on the same day that the vaccinator collects the monthly supply of all vaccines from a higher level.

• The relatives of the expectant mother may collect the vaccine from the nearest health centre that stores the vaccine within or outside the cold chain, to be given to the midwife to administer after delivery.

• The child may be taken after birth to a nearby health facility with continuous availability of the vaccine. However, programmatically, it is best if health workers take the responsibility to provide the birth dose at the birthing place, rather than giving responsibility to the parents, who might not follow through.

2. Train midwives.

All midwives attending births and competent to provide injections should be provided training in handling, storing and transporting hepatitis B vaccine out of the cold chain. In addition, their training should include the list of topics provided in the training checklist in Box 9.

3. Record and report birth doses.

Sufficient child-held immunization cards should be made available to midwives attending births. Midwives should take the cards with them as part of their midwifery kits and give the cards to the parents. Midwives should also submit to the EPI staff of the health facility a monthly report on the number of births attended and the number of birth doses administered.

Figure 9. Prefilled Uniject devices (with attached VVM), with hepatitis B vaccine stored outside the cold chain, as part of the midwifery kit, can increase the coverage of hepatitis B birth dose for home deliveries with trained attendance.
At-home births delivered by untrained attendants:

Although every effort should be made to increase access to trained delivery care, the following approaches should be used in the interim for those infants who are delivered by untrained attendants:

1. **Ensure the availability of the vaccine.**
   - If the mother comes in contact with a health worker during the antenatal period, the health provider must inform the mother about the need for an early dose of hepatitis B vaccine and tell her whom to contact after delivery to get the dose.
   - Traditional birth attendants should be involved in the immunization programme. If they are not competent to give the injections themselves, they should inform the health facility as soon as possible about the birth, so that a health worker can provide the vaccine through an outreach visit.
   - Community notification of births. Mothers and other household members should be encouraged to inform the health facility about an upcoming birth. Health workers should try to administer the vaccine through an outreach visit at the earliest possible opportunity.
   - Mothers or other household members should be encouraged to take the baby to the nearest health centre to get the injection. **Vaccines, in or out of cold chain should be stored in health facilities at all times.**

2. **Train maternal health services staff using the checklist in Box 9.**

3. **Other operational elements.**

A health worker should be clearly designated to provide hepatitis B vaccine to newborn infants at home after being informed about births. The operational costs to conduct outreach services, based on the estimated number of such births, should be clearly provided for in the budget of the health facility.
Instructions to Health Workers If Child First Comes in Contact After 24 Hours Despite All Efforts to Reach Early

Although every effort should be made to give the birth dose within 24 hours, the vaccine may provide some protection if given after this period. Hence, in instances where despite all efforts, the child first comes in contact with health systems after 24 hours of births, the instruction to the health workers should be:

A. *In countries using monovalent hepatitis B vaccine:* Give the first dose of hepatitis B vaccine at the first opportunity when the child comes in contact with the health systems. Give the second dose at least one month after the first dose. For example, if a child comes in contact with the health systems for the first time 21 days after birth—give the child the first dose of hepatitis B vaccine immediately and schedule his 2nd dose of hepatitis B vaccine at least one month after that (or to save visits, the 2nd dose can be scheduled with 2nd dose of DPT rather than with first dose of DPT, and third dose with third dose of DPT)

B. *In countries using combination vaccines:* The instruction to the health worker in countries using combination vaccine should be:

> Give one dose of monovalent hepatitis B vaccine as early as possible after birth, preferably within 24 hours of birth. However, do not deny a dose of monovalent hepatitis B vaccine if the child first comes into contact with the health system after the 24-hour period and before the child is old enough to be given the first dose of combination vaccine.

For example if a child comes in contact with the system on 30th day after birth—he is still not old enough to receive the combination vaccine (generally given at 6 wks of age)—give him a dose of monovalent hepatitis B. Afterwards follow the combination vaccine schedule as usual.
5. Side-Effects and Contraindications

There are no contraindications for the administration of hepatitis B vaccine to a newborn infant within 24 hours of birth. In many developing countries, neonatal mortality remains high, either because of poor delivery care or poor neonatal care practices. In such countries, there is a high likelihood of a coincidental association between the administration of the birth dose and neonatal complication or death due to other causes. Such a coincidence may lead to hesitation on the part of health workers to administer the vaccine, or may lead to general negative perceptions about immunization, as expressed by health workers in a study conducted in Indonesia and Viet Nam.

In a large case-control study conducted in New Zealand, no evidence was found that vaccination with hepatitis B vaccine increased the risk of sudden infant death syndrome (SIDS). Moreover, no increase has been observed in the frequency of reported adverse events, including SIDS, since the implementation of routine infant hepatitis B vaccination in the United States of America. Infant death rates, including rates of SIDS, declined substantially in the United States during the 1990s, while infant hepatitis B vaccination coverage increased from less than 1% to more than 90%.

Although fever may occasionally occur after hepatitis B vaccination, administration of the vaccine soon after birth has not been associated with an increase in the number of febrile episodes or sepsis evaluations.

Low birth weight or premature delivery are not contraindications of hepatitis B vaccine, although health staff may hesitate to give the vaccine due to increased risk of death in low-birth-weight and premature neonates on account of other reasons. However, if the birth weight is less than 2000 grams, the vaccine dose at birth should not be counted towards the primary series, and three additional doses should be given.

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### Annex 1

**Place of birth: Percentages in The Western Pacific Region, 2005**

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<th>COUNTRY</th>
<th>Total population (000s)</th>
<th>Crude birth rate/1000 population</th>
<th>Total births</th>
<th>% of total births in the Region</th>
<th>% of births in a health facility</th>
<th>Number of births outside a health facility</th>
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<td>74 449</td>
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<td>1 718 978</td>
<td>13</td>
<td>23 076 979</td>
<td>100.00</td>
<td>70.5</td>
<td>6 796 333</td>
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</tbody>
</table>

Source: The data is compiled from different sources including www.childinfo.org and data bases maintained by WPRO.
Annex 2

Outcome of HBV Infection

Perinatal infection

- Asymptomatic (99%)
- Symptomatic (1%)

No perinatal infection

Early childhood infection

- Asymptomatic (90%)
- Symptomatic (10%)

Late infection

- Asymptomatic (70%)
- Symptomatic (30%)

Key

S: Acute hepatitis B
C: Chronic infection

90% chronic

Chronic (90%)
Resolved (10%)

30% chronic

Chronic (30%)
Resolved (70%)

6% chronic

Chronic (6%)
Resolved (6%)

Source: CDC, Atlanta, USA

1 Based on prevalence of HBV infection at 5 years old
2 Based on prevalence of HBV infection at >30 years old
Annex 3


1. Demonstration of thermostability of hepatitis B vaccine through laboratory testing

HB vaccine is relatively heat stable and undergoes only a small loss of potency when stored for two to six months at 37° Celsius. WHO considers HB vaccine to be a candidate for use beyond the cold chain under certain conditions because of its thermal stability and vulnerability to damage due to freezing during storage and transport\(^\text{10}\).

Sutanto et al\(^\text{11}\) also reported potency testing results for hepatitis B vaccine stored at a typical field site for one month (average temperature 27° Celsius, range 25°-32°). The vaccine suffered a 1% drop in potency (cold chain samples 100% relative potency; ambient temperature storage samples: 99% relative potency). It thus remained within the potency limits established by the testing authority (Indonesian National Quality Control Laboratory for Drug and Food and the National Center for Disease Research and Development).

2. Demonstration of heat stability of hepatitis B vaccine under service—delivery conditions

2.1 Studies in China

Long-An County, China, 1991\(^\text{12}\)

Hepatitis B vaccine stored at room temperature was given to 358 infants at birth by village midwives. As a control, the same vaccine, stored in a refrigerator, was administered to 232 infants within 24 to 72 hours of birth by village doctors. The 2nd and 3rd doses were given with other vaccines as part of mobile outreach services, which were available at intervals of about two months. The rates of seroconversion to antiHBs for vaccines stored without was 81.6% and with refrigeration, 81.9%.

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\(^{10}\) Regional Plan to improve hepatitis B control through immunization. Manila, World Health Organization, Regional Office for the Western Pacific, 2003.


Hainan Province, China, 2005

This study assessed the effectiveness and safety of the hepatitis B vaccine-Uniject out of cold chain for improving the timeliness of first dose of hepatitis B vaccine in remote areas of China with high rates of home births. Out of 143 children involved in serological survey, 96% had anti-HBS seroconversion and 95% had levels defined as protective. The anti-HBs seroconversion rates were similar for infants receiving an HB vaccine stored within the cold chain, out of the cold chain for 14 or fewer days, or out of the cold chain for 15 to 30 days. All hepatitis B vaccine-Uniject stored both inside and outside the cold chain were labelled with vaccine vial monitors (VVM) to identify possible excessive time-heat exposure.

Hunan Province, China, 2005

The project areas were divided into three groups. In Group one, (vaccine was provided according to the current practice) vaccine in ampoules was distributed through the cold chain and stored at village doctors’ offices in vaccine carriers with icepacks for the usual time of three days. No vaccine was available for the rest of the days. In Group 2, hepatitis B vaccine ampoules with attached VVMs were distributed through the cold chain to village doctors’ offices, where they were stored in a protected place at ambient temperatures for up to one month, so that the vaccine was available near to the place of delivery of newborn infants in the village. In Group 3, Uniject devices with VVM labels and prefilled with vaccine were distributed and stored in the same way as Group 2. Of the 606 children involved in the serological survey, 96% had anti-HBs, and among those 94% had levels defined as protective (i.e. ≥10 mIU/ml). The geometric mean titre (GMT) ranged from 93 to 102 mIU/ml, with no significant differences between the three groups.


2.2 Studies in Indonesia (Tabanan District, Bali)

Project areas were divided into three groups. Group 1 was given their first dose of HB vaccine with Uniject stored out of the cold chain, group 2 with Uniject stored in the cold chain, and group 3 with standard syringe, needle and multidose vials stored in the cold chain. Subsequent doses were given by the usual means and blood samples were drawn 4-6 weeks after the third dose was given. No significant differences were found in seroconversion rates or geometric means titres (GMT) of anti-HBs between the three groups.

2.3 Studies in Viet Nam

The immunogenicity of three doses of a local plasma-derived vaccine was compared among infants who received three doses stored in cold chain (n=358) or from whom the first dose was stored out of the cold chain for up to one month (n=748). Serum was collected at age 9-18 months, and the vaccine was found to be protective in 80.3% of all infants. There were no differences in the prevalence of a protective level of antibodies or geometric means titres (GMT) between the two groups.

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Annex 4

Anticipated Seroprevalence in the Western Pacific Region If no Birth Doses Were to be Given

[Based on model developed by author of these guidelines]

The birth dose is essential to achieving the less than 2% seroprevalence goal by 2012 and the ultimate regional goal of less than 1% seroprevalence.

Total number of births in non-Pacific Island Countries in 2004

23 002 530

Number of mothers positive for HbsAg at the rate of 10% seroprevalence for HbsAg

23 002 53

HbsAg-positive but HbeAg-negative (60% of total)

1 380 152

Risk of infection (10%)

138 015

Risk of becoming a carrier (90%)

869 494

Average infant mortality rate 30/1000 births (25 302 children will die from unrelated causes)

869 494 carrier one year-olds every year or 3.7% carrier rate
## Annex 5

Anticipated Seroprevalence in the 2004 Birth Cohort Based on Reported Birth Dose and HepB3 Coverage in Various Countries and Areas of the Western Pacific Region

[Based on model developed by author of these guidelines]

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>HBsAg+ pregnant women (%)</th>
<th>HbeAg*+ pregnant women (%)</th>
<th>Perinatal infections in the absence of a birth dose</th>
<th>Birth dose coverage (%)</th>
<th>Estimated number of births infected, with the current birth dose coverage **</th>
<th>HepB3 coverage % (JRF 2005)</th>
<th>Expected HBsAg level in 5 year-olds born in 2004 (%)</th>
<th>Expected HBsAg levels due to perinatal infection (%)</th>
<th>Share of seroprevalence due to perinatal transmission out of total (%)</th>
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### Assumptions in the model:
- Seroprevalence among pregnant women is the same as that in general population.
- 40% seropositivity for HbeAg among HbsAg + women.
- 10% perinatal transmission risk among women positive only for HBsAg.
- 90% transmission risk among women positive for both HBsAg and HBeAg.
- 95% vaccine efficacy for prevention of both perinatal and horizontal transmission.
- Unprotected children will achieve the same carriage rate at the end of five years as observed in the general population.
- The model does not take into account the reduced risk of horizontal transmission over time due to overall economic development and improvements in health delivery systems, especially injection safety.
- The model also does not take into account the reduced risk of horizontal transmission due to reduced perinatal transmission and herd immunity.
Annex 6

Sample Communication Messages for the Mass Media, Targeted Towards Health Workers and Parents

4 out of 10 hepatitis B carriers become infected at birth

But it is preventable.

Give first dose of hepatitis B vaccine within 24 hours of birth

For full protection against hepatitis B, a total of 3 doses of hepatitis vaccine will be required at an interval of at least one month.

Photos by: WHO/WPRO Image Bank, Manju Rani and David Hipgrave