

# Hepatitis B immunization

## *Introducing hepatitis B vaccine into national immunization services*

### Background

Hepatitis B (HepB) is a major public health problem worldwide. Approximately 30% of the world's population, or about 1.8 billion persons, have serologic evidence of hepatitis B virus (HBV) infection. Of these, an estimated 350 million have chronic HBV infection and at least 500 000 chronically infected persons die each year from liver cancer and cirrhosis. HBV is second only to tobacco as a known human carcinogen.

A safe and effective vaccine against HBV infection has been available for nearly 20 years. HepB vaccine is effective in preventing HBV infections when it is given either before exposure or shortly after exposure. At least 85%-90% of HBV-associated deaths are vaccine-preventable.

WHO recommends that HepB vaccine be included in routine immunization services in all countries. This document provides an outline of information needed to implement a national decision to introduce HepB vaccine, with a particular focus on issues relevant to countries applying for support for the introduction of HepB vaccine from The Vaccine Fund.

### Objective

The primary objective of HepB immunization is to prevent chronic HBV infections which result in chronic liver disease later in life. By preventing chronic HBV infections, the major reservoir for transmission of new infections is also reduced.

### Immunization strategies

Routine infant immunization. HepB immunization of all infants as an integral part of the national immunization schedule should be the highest priority in all countries. Additional immunization strategies that should be considered depending on the epidemiology of HBV transmission in a particular country are:

- *Prevention of perinatal HBV transmission.* In order to prevent HBV transmission from mother to infant, the first dose of HepB vaccine needs to be given as soon as possible after birth (preferably within 24 hours). In countries where a high proportion of chronic infections is acquired perinatally (e.g. South-East Asia), a birth dose should be given to infants. It is usually most feasible to give HepB vaccine at birth when infants are born in hospitals. Efforts should also be made in these countries to give HepB vaccine



## DEPARTMENT OF VACCINES AND BIOLOGICALS



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as soon as possible after delivery to infants delivered at home. In countries where a lower proportion of chronic infections is acquired perinatally (e.g. Africa), the highest priority is to achieve high DTP3 and HepB3 vaccine coverage among infants. In these countries, use of a birth dose may also be considered after disease burden, cost-effectiveness, and feasibility are evaluated.

- *Catch-up vaccination of older persons.* (Note: The Vaccine Fund does not provide vaccine for catch-up immunization). In countries with a high endemicity of chronic HBV infection (hepatitis B surface antigen [HBsAg] prevalence  $\geq 8\%$ ), catch-up immunization is not usually recommended because most chronic infections are acquired among children <5 years of age, and thus, routine infant vaccination will rapidly reduce HBV transmission. In countries with lower endemicity of chronic HBV infection, a higher proportion of chronic infections may be acquired among older children, adolescents and adults; catch-up immunization for these groups may be considered.

## Vaccine formulations

HepB vaccine is available in monovalent formulations that protect only against HBV infection and also in combination formulations that protect against HBV and other diseases.

- Monovalent HepB vaccines *must be used* to give the birth dose of HepB vaccine.
- Combination vaccines that include HepB vaccine must not be used to give the birth dose of HepB vaccine because DTP and Hib vaccines are not recommended to be given at birth.
- Either monovalent or combination vaccines may be used for later doses in the HepB vaccine schedule. Combination vaccines can be given whenever all of the antigens in the vaccine are indicated.

## Schedule

HepB vaccine schedules are very flexible; thus, there are multiple options for adding the vaccine to existing national immunization schedules without requiring additional visits for immunization.

Programmatically, it is usually easiest if the 3 doses of HepB vaccine are given at the same time as the 3 doses of DTP (Option I). This schedule will prevent

infections acquired during early childhood, which account for most of the HBV-related disease burden in high endemic countries, and also will prevent infections acquired later in life. However, this schedule will not prevent perinatal HBV infections because it does not include a dose of HepB vaccine at birth. Two schedule options can be used to prevent perinatal HBV infections: a 3-dose schedule of monovalent HepB vaccine, with the 1<sup>st</sup> dose given at birth and the 2<sup>nd</sup> and 3<sup>rd</sup> doses given at the same time as the 1<sup>st</sup> and 3<sup>rd</sup> doses of DTP vaccine (Option II); or a 4-dose schedule in which a birth dose of monovalent HepB vaccine is followed by 3 doses of a combination vaccine, e.g. DTP HepB (Option III). The 3-dose schedule (Option II) is less expensive, but may be more complicated to administer, because infants receive different vaccines at the 2<sup>nd</sup> immunization visit than at the 1<sup>st</sup> and 3<sup>rd</sup> visits. The 4-dose schedule (Option III) may be easier to administer programmatically, but is more costly, and vaccine supply issues may make it unfeasible.

## Administration

HepB vaccine is given by intramuscular injection in the anterolateral aspect of the thigh (infants) or deltoid muscle (older children). It can safely be given at the same time as other vaccines (e.g. DTP, Hib, measles, OPV, BCG, and yellow fever). If HepB vaccine is given on the same day as another injectable vaccine, it is preferable to give the two vaccines in different limbs.

## Injection equipment

The injection equipment for HepB vaccine is the same type as that for all other EPI vaccines (except for BCG vaccine):

Options for adding hepatitis B vaccine to childhood immunization schedules

		Hepatitis B vaccine options					
		No birth dose			With birth dose		
Age	Visit	Other antigens			I	II	III
Birth	0	BCG [OPV0] <sup>1</sup>				HepB -birth <sup>2</sup>	HepB -birth <sup>2</sup>
6 weeks	1	OPV1	DTP1	Hib1	HepB1 <sup>3</sup>	HepB2 <sup>2</sup>	DTP-HepB1 <sup>4</sup>
10 weeks	2	OPV2	DTP2	Hib2	HepB2 <sup>3</sup>		DTP-HepB2 <sup>4</sup>
14 weeks	3	OPV3	DTP3	Hib3	HepB3 <sup>3</sup>	HepB3 <sup>2</sup>	DTP-HepB3 <sup>4</sup>
9–12 months	4		Measles		Yellow fever		

<sup>1</sup> only given in high polio endemic countries  
<sup>2</sup> monovalent vaccine  
<sup>3</sup> monovalent or combination vaccine  
<sup>4</sup> combination vaccine

- 0.5 ml auto-disable (AD) syringes are recommended.
- In immunization services where sterilizable syringes are still used, a 0.5ml sterilized syringe should be used.
- If neither AD or sterilizable syringes are available, standard disposable syringes (1.0ml or 2.0ml) must be used ONCE ONLY, and safely disposed of after use.
- A 25 mm, 22 or 23 gauge needle is recommended.

## Dosage

The standard paediatric dose is 0.5 ml.

## Vaccine procurement

In most countries, HepB vaccine procured through The Vaccine Fund will be supplied through the UNICEF procurement mechanism. The number of HepB vaccine doses required is estimated using the size of the birth cohort, the coverage rate for DTP and the number of doses in the immunization schedule. These calculations should also include wastage and the size of the reserve stock.

## Presentation

HepB vaccines are available in liquid single-dose and multi-dose glass vials, and in pre-filled single-dose injection devices (e.g. Uniject™).

## Storage and shipping volume

Storage volumes (vial plus packet containing vial plus other packaging) for HepB vaccines supplied through UNICEF are as per the figure below:

For comparison, the total storage volume for other EPI vaccines (BCG, DTP, measles, OPV, TT) is about 11.0 cm<sup>3</sup> per dose.

## Cold chain issues

The storage temperature for HepB vaccine is the same as for DTP vaccine, from 2°C to 8°C. *HepB vaccine should never be frozen.* If frozen, HepB vaccine loses its potency.

Adding HepB vaccine to the national immunization schedule will require cold chain assessments at all administrative levels:

- to assure adequate storage capacity is available, and
- to assure policies and procedures are in place to prevent freezing of HepB vaccine.

## Reducing vaccine wastage

Since hepatitis B vaccines are more expensive than the traditional EPI vaccines, it is important to monitor HepB vaccine wastage and to develop and implement strategies to reduce wastage. Strategies to reduce wastage include:

- careful planning of vaccine ordering and distribution;
- implementation of WHO's multi-dose vial policy;
- appropriate use of single-dose and multi-dose vials;
- careful maintenance of the cold chain;
- attention to vaccine security; and
- reducing missed opportunities for immunization.

## Injection safety

HepB vaccine procured through The Vaccine Fund will be supplied with AD syringes and safety boxes. Managers at each level are responsible for ensuring that adequate supplies are available at all times so that each injection is given with a sterile injection device. Attention should also be given to proper use and disposal of safety boxes to collect these materials.

## Revision of Immunization forms and materials

An important element of integrating HepB vaccine into national immunization programmes is to revise training and informational materials, immunization cards and forms used to monitor and evaluate immunization services.

## Training

Training for health care staff is essential because these staff are responsible for handling and administering HepB vaccine and they are a major source of information for parents and others in the general public.

## Advocacy and communication

Advocacy and communication efforts are important in order to generate support and commitment for the new vaccine. The primary target audiences are decision-makers/opinion leaders, health care staff, and the general public (including parents).

Vaccine	Packed volume per dose cm <sup>3</sup>			
	1 dose vials	2 dose vials	6 dose vials	10 dose vials
HepB monovalent	9.7-14.9	4.8	3.2	3.0
HepB (Uniject™)	24.6	—	—	—
HepB + DTP (packaged together)	—	—	—	8.2
DTP-HepB (combined)	—	—	—	3.0
DTP-HepB+Hib	—	9.7	—	—

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## What information is needed to assess HepB disease burden?

Adequate seroprevalence data needed to assess HepB disease burden are generally available in all countries, or from adjacent countries with similar HBV endemicity. Thus, additional seroprevalence studies are usually not needed.

## How should HepB vaccine be phased into the existing infant immunization services?

A strategy in which HepB vaccine is given to infants who have not yet completed the DTP vaccine series at the time HepB vaccine is introduced is generally the most feasible to implement.

## Are monovalent or combination vaccines most suitable?

Issues to consider in choosing a suitable HepB vaccine for national immunization schedules include: flexibility in adding the vaccine to the national immunization schedule; impact on cold chain capacity; the number of injections per visit; vaccine security; impact on local vaccine production; and cost. Use of combination vaccines (e.g. DTP-HepB vaccine) may offer certain programmatic advantages. These include:

- a decreased number of injections required per visit (and thus decrease the number of needles and syringes required); and
- a decrease in the amount of space required for cold chain storage and transport.

## How can the addition of HepB vaccine be used to strengthen national immunization services?

HepB vaccine introduction should be used as an opportunity to strengthen existing immunization services. Issues needing particular attention include stock management, reducing vaccine wastage, injection safety, and monitoring coverage.

## Budgeting for HepB vaccine introduction

Capital and recurrent costs related to the introduction of HepB vaccine should be estimated and included in the annual immunization budget. Additional capital costs might include investment in cold chain equipment and information campaigns targeted to the general public. Additional recurrent costs include vaccines, AD syringes, training, safe disposal of waste, and evaluation of the impact of immunization.

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