DESCRIPTION
The vaccine is a homogeneous liquid containing purified diphtheria and tetanus toxoids, inactivated whooping cough (pertussis) organisms, highly purified, non-infectious particles of hepatitis B surface antigen (HBsAg) and Hib component as a bacterial subunit vaccine containing highly purified, non-infectious Haemophilus influenzae type b (Hib) capsular polysaccharide chemically conjugated to a protein ……..(specify). The HBsAg is produced by DNA recombinant technology in yeast/mammalian (state which) cells. The vaccine is adsorbed on to …….. (specify). …… (specify) is used as a preservative (specify amount per dose). The polysaccharide is derived from Hib bacteria grown in chemically defined media, and subsequently purified through a series of ultrafiltration steps. …… The potency of the vaccine per single human dose is at least 4 IU for pertussis, 30 IU for diphtheria, 60 IU for tetanus (determined in mice) or 40 IU (determined in guinea pig) and …. HBsAg (in vivo test) and …….. µg/ml Hib.

COMPOSITION

<table>
<thead>
<tr>
<th>Paediatric Dose</th>
<th>Volume</th>
<th>Diphtheria toxoid</th>
<th>Tetanus toxoid</th>
<th>Pertussis antigen</th>
<th>Hepatitis B surface antigen</th>
<th>Hib conjugate</th>
<th>Nature of Aluminium salt and quantity as AL+++</th>
<th>Nature and amount of preservatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>xx Lf/ml (…..IU/ml)</td>
<td>0.5 ml</td>
<td>xx Lf/ml (…..IU/ml)</td>
<td>XX OU/ml</td>
<td>XX µg/ml</td>
<td>XX µg/ml</td>
<td>XX mg/ml</td>
<td>XX mg/ml</td>
<td></td>
</tr>
</tbody>
</table>

ADMINISTRATION
The liquid vaccine vial should be shaken before use to homogenize the suspension. The vaccine should be injected intramuscularly. The anterolateral aspect of the upper thigh is the preferred site of injection. An injection into a child’s buttocks may cause injury to the sciatic nerve and is not recommended. It must not be injected into the skin as this may give rise to local reaction. One paediatric dose is 0.5ml. A sterile syringe and sterile needle must be used for each injection.

IMMUNIZATION SCHEDULE
DTwP-HepB-Hib vaccine should NOT be used for the birth dose.

In countries where pertussis is of particular danger to young infants, the combination vaccine should be started as soon as possible with the first dose given as early as 6 weeks, and two subsequent doses given at 4-week intervals.

The DTwP-HepB-Hib vaccine can be given safely and effectively at the same time as BCG, measles, polio (OPV or IPV), and yellow fever vaccines and vitamin A supplementation. If DTwP-HepB-Hib vaccine is given at the same time as other vaccines, it should be
administered at a separate site. It should not be mixed in the vial or syringe with any other vaccine unless it is licensed for use as a combined product.

**SIDE EFFECTS**

The type and rate of severe adverse reactions do not differ significantly from the DTwP, HepB and Hib vaccine reactions described separately.

For DTwP, mild local or systemic reactions are common. Some temporary swelling, tenderness and redness at the site of injection together with fever occur in a large proportion of cases. Occasionally severe reactions of high fever, irritability and screaming develop within 24 hours of administration. Hypotonic-hyporesponsive episodes have been reported. Febrile convulsions have been reported at a rate of one per 12500 doses administered. Administration of acetaminophen at the time and 4-8 hours after immunization decreases the subsequent incidence of febrile reactions. The national childhood encephalopathy study in the United Kingdom showed a small increased risk of acute encephalopathy (primarily seizures) following DTP immunization. However subsequent detailed reviews of all available studies by a number of groups, including the United States Institute of Medicine, the Advisory Committee on Immunization Practices, and the paediatric associations of Australia, Canada, the United Kingdom and the United States, concluded that the data did not demonstrate a causal relationship between DTwP and chronic nervous system dysfunction in children. Thus there is no scientific evidence that these reactions have any permanent consequences for the children∗.

Hepatitis B vaccine is very well tolerated. In placebo-controlled studies, with the exception of local pain, reported events such as myalgia and transient fever have not been more frequent than in the placebo group. Reports of severe anaphylactic reactions are very rare. Available data do not indicate a causal association between hepatitis B vaccine and Guillain–Barré syndrome, or demyelinating disorders including multiple sclerosis, nor is there any epidemiological data to support a causal association between hepatitis B vaccination and chronic fatigue syndrome, arthritis, autoimmune disorders, asthma, sudden infant death syndrome, or diabetes.

Hib vaccine is very well tolerated. Localized reactions may occur within 24 hours of vaccination, when recipients may experience pain and tenderness at the injection site. These reactions are generally mild and transient. In most cases, they spontaneously resolve within two to three days and further medical attention is not required. Mild systemic reactions, including fever, rarely occur following administration of Hib vaccines. More serious reactions are very rare; a causal relationship between more serious reactions and the vaccine has not been established.

**CONTRAINDICATIONS**

Known hypersensitivity to any component of the vaccine, or a severe reaction to a previous dose of the combination vaccine or any of its constituents is an absolute contraindication to subsequent doses of the combination vaccine or the specific vaccine know to have provoked an adverse reaction. There are few contraindications to the first dose of DTwP - fits or abnormal cerebral signs in the newborn period or other serious neurological abnormality are

∗ In Weekly Epidemiological Record, No. 18, 7 May 1999. Page 139
contraindications to the pertussis component. In this case, the vaccines should not be given as a combination vaccine but DT should be given instead of DTwP and Hep B and Hib vaccines given separately. The vaccine will not harm individuals currently or previously infected with the hepatitis B virus.

**Immune deficiency**
Individuals infected with the human immuno-deficiency virus (HIV), both asymptomatic and symptomatic, should be immunized with combined vaccine according to standard schedules.

**STORAGE**
The components of the combination vaccine must be stored and transported between $+2^\circ$C and $+8^\circ$C. **The DTwP-HEP B-Hib vaccine MUST NOT BE FROZEN.**
Multi-dose vials of vaccine from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 4 weeks, provided that all of the following conditions are met (as described in the *WHO policy statement: The use of opened multi dose vials in subsequent immunization sessions. WHO/V&B/00.09)*:

- The expiry date has not passed;
- The vaccines are stored under appropriate cold chain conditions;
- The vaccine vial septum has not been submerged in water;
- Aseptic technique has been used to withdraw all doses;
- The vaccine vial monitor (VVM), if attached, has not reached the discard point (see figure).

**PRESENTATION**
The vaccine comes in single dose vials or vials of .... (specify) doses.
Vaccine Val Monitors (VVMs) are part of the label on ……..(specify vaccine) supplied through ………(specify supplier or manufacturer). The colour dot which appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level. The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, then the vial should be discarded.