Statement of Intent

This guideline is meant to be a guide for clinical practice, based on the best available evidence at the time of development. Adherence to this guideline may not necessarily ensure the best outcome in every case. Every health care provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

Review of the Guidelines

This guideline was issued in September 2004 and will be reviewed in September 2006 or sooner if new evidence becomes available.

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Available on the following website: http://www.moh.gov.my
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GUIDELINES DEVELOPMENT AND OBJECTIVES

Guideline Development
The work group for the development of these guidelines comprised paediatricians from various Ministry of Health facilities. These guidelines are based on the findings of health technology assessment on the same topic, as well as a systematic review of current medical literature. The ranking of evidence is based on a modified version of that suggested by the Catalonia Agency for Health Technology Assessment and Research (CAHTAR) Spain, while the grading of recommendations in these guidelines emulates that used by the Scottish Intercollegiate Guidelines Network (SIGN). The draft guidelines were posted on both the Ministry of Health Malaysia and Academy of Medicine, Malaysia websites for comment and feedback. These guidelines have also been presented to the Technical Advisory Committee for Clinical Practice Guidelines and Health Technology Assessment and Clinical Practice Guidelines Council, Ministry of Health Malaysia for review and approval.

Objective
The aim of this guideline is to aid health care providers in general practice and pediatricians, in clinical decision making by providing well-balanced evidence based information on childhood immunisation. It also hoped to decrease the incidence of complications.

Target Population
This guideline is developed to apply to all children.

Target Group
This guideline is meant for all health care providers.
### LEVEL OF EVIDENCE SCALE

<table>
<thead>
<tr>
<th>Level</th>
<th>Strength of evidence</th>
<th>Study design</th>
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<tbody>
<tr>
<td>1</td>
<td>Good</td>
<td>Meta-analysis of RCT, Systematic review</td>
</tr>
<tr>
<td>2</td>
<td>Good</td>
<td>Large sample RCT</td>
</tr>
<tr>
<td>3</td>
<td>Good to Fair</td>
<td>Small sample RCT</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>Non-randomised controlled prospective trial</td>
</tr>
<tr>
<td>5</td>
<td>Fair</td>
<td>Non-randomised controlled prospective trial with historical control</td>
</tr>
<tr>
<td>6</td>
<td>Fair</td>
<td>Cohort studies</td>
</tr>
<tr>
<td>7</td>
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<td>8</td>
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</tr>
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<td>9</td>
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<td>Expert committees, consensus, case reports, anecdotes</td>
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</tbody>
</table>

(Adapted from Catalanian Agency for Health Technology Assessment & Research, [CAHTAR] Spain)

### GRADE OF RECOMMENDATIONS

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<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At least one meta analysis, systematic review, or RCT, or evidence rated as good and directly applicable to the target population</td>
</tr>
<tr>
<td>B</td>
<td>Evidence from well conducted clinical trials, directly applicable to the target population, and demonstrating overall consistency of results; or evidence extrapolated from meta analysis, systematic review, or RCT</td>
</tr>
<tr>
<td>C</td>
<td>Evidence from expert committee reports, or opinions and/or clinical experiences of respected authorities; indicates absence of directly applicable clinical studies of good quality</td>
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(Adapted from Scottish intercollegiate Guidelines Network [SIGN])
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<td>20</td>
</tr>
<tr>
<td>1.2 Mumps</td>
<td>20</td>
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<td>3. VACCINE EFFICACY</td>
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<td>4. STORAGE, DOSAGE AND ROUTE OF ADMINISTRATION</td>
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CHILDHOOD IMMUNISATION

Immunisation is an attempt to replace the anticipated natural primary contact between the human body and a hostile organism, with a safer artificial contact, so that any subsequent natural contact takes place in a state of heightened immunity. While advances in public health and medicine have reduced the morbidity and mortality rates accompanying certain infectious diseases, immunisation represents the single-most mass approach to prevention (Zimmerman, 1987).

The World Health Organisation (WHO) Expanded Programme on Immunisation (EPI) recommends that all countries immunise against poliomyelitis, diphtheria, pertussis, tetanus, measles, and tuberculosis (TB) infection in countries with a high incidence. In addition, Hepatitis B vaccine was to be integrated into national immunisation programmes in all countries by 1997 (Ministry of Health Malaysia, 2002, level 1).

Table 1: EPI schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccine</th>
<th>Hepatitis B Vaccine**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Scheme A</td>
</tr>
<tr>
<td>Birth</td>
<td>BCG, OPV 0</td>
<td>HB1</td>
</tr>
<tr>
<td>6 weeks</td>
<td>DPT 1 OPV 1</td>
<td>HB 2</td>
</tr>
<tr>
<td>10 weeks</td>
<td>DPT 2, OPV 2</td>
<td>HB 3</td>
</tr>
<tr>
<td>14 weeks</td>
<td>DPT 3, OPV 3</td>
<td></td>
</tr>
<tr>
<td>9 months</td>
<td>Measles, Yellow fever*</td>
<td></td>
</tr>
</tbody>
</table>

* In countries where yellow fever poses a risk
** Scheme A is recommended for countries where perinatal transmission of hepatitis B virus is frequent (e.g. South Asia), while scheme B is for those with less frequent perinatal transmission (e.g. Sub-Saharan Africa)

It has generally been accepted that no immunisation schedule is ideal, and thus the EPI recommends that each country determine its own schedule that best suits its needs. The strategic guiding principle of any immunisation programme is that protection must be achieved before infants are at high risk of a disease. In most developing countries, diseases included within the EPI strike early in life, and thus it is important to protect children through immunisation as early as possible. Apart from this, any immunisation schedule represents some degree of compromise. In addition, while acknowledging that seroconversion is age-dependent, the emphasis should be on obtaining protection in the infant at as young an age as possible (Ministry of Health Malaysia, 2002, level 1).

The immunisation programme in Malaysia commenced about 40 years ago with the DPT vaccine. This was followed by the BCG vaccine in 1961 and the OPV vaccine in 1972. Measles immunisation was added
to the programme in 1984, with immunisation against rubella being introduced in 1988 and against hepatitis B in 1989 (Pathmanathan, 1990). The immunisation coverage for Malaysia was 99.97% for BCG, 95.3% for DPT (third dose), 95.4% for OPV (third dose), 88.4% for measles and 93.5% for hepatitis B (third dose) in 2000 (Ministry of Health Malaysia, 2002, level 1). The new recommended immunisation schedule is as illustrated in Table 2 below:

Table 2: New immunisation schedule.

<table>
<thead>
<tr>
<th>Immunisation</th>
<th>Age (months)</th>
<th>Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 1 2 3 4 5 6 12 18 6</td>
<td>No scar DT</td>
</tr>
<tr>
<td>BCG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hep B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DPT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hib</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMR</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*for Sabah only

For immunodeficient children, the recommended schedule is shown below:

Table 3 Recommended Immunisation Schedule for Immunodeficient Children

<table>
<thead>
<tr>
<th>Immunisation</th>
<th>Immunosuppressive therapy</th>
<th>HIV</th>
<th>Sibling/Close Contacts</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Hep B</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>DPT</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>OPV</td>
<td>No</td>
<td>Yes [IPV (killed vaccine)]</td>
<td>Yes (IPV)</td>
</tr>
<tr>
<td>Hib</td>
<td>Yes (3 + Booster dose)</td>
<td>Yes (3 + Booster dose)</td>
<td>Yes (3 + Booster dose)</td>
</tr>
<tr>
<td>Measles</td>
<td>No</td>
<td>Yes (Asymptomatic)</td>
<td>Yes</td>
</tr>
<tr>
<td>MMR</td>
<td>No</td>
<td>Yes (Asymptomatic)</td>
<td>Yes</td>
</tr>
</tbody>
</table>
BCG VACCINE

1. INTRODUCTION

In Malaysia, the incidence of tuberculosis was 63.6 per 100,000 population in 1997, and has been increasing steadily since 1995. The most important source of human infection is an infected person who spreads the highly infectious bacilli through respiratory droplets. Primary infections occur at any age, most often in children, may be asymptomatic, and resolve spontaneously. However, it may also spread and cause disease in various organs including lungs, meninges, bones and bloodstream (Ministry of Health Malaysia, 2002, level 1).

The Bacille Calmette-Guerin (BCG) vaccine is a live attenuated strain of Mycobacterium bovis, containing no adjuvant or preservative except monosodium glutamate or albumin as the stabilizer. The diluent is either saline solution or distilled water. WHO recommends that it be administered at birth, and it is currently used in more than 100 countries (WHO, 2000, level 1).

2. ADVERSE EFFECTS

Following intra-dermal injection, local reaction is normal, a papule forming within 2-3 weeks, with ulceration at 6-8 weeks, followed by a scar at the end of 3 months. The adverse events are predominantly related to infection by the live attenuated bacteria, as well as being due to errors in achieving intra-dermal inoculation. They can be classified as mild and severe events and are elaborated on below.

2.1 Mild Adverse Events

The most common adverse effect of subcutaneous injection is a local abscess. While more extensive and prolonged local reactions can occur, secondary infections at the site of injections are unlikely. Sometimes, axillary or cervical lymphadenitis may develop. However, in most cases it heals spontaneously, and no treatment is required. In extreme cases, systemic treatment with erythromycin for up to one month may be helpful. In cases with adherent or fistulated lymphadenitis, drainage may be carried out and anti-tuberculous drugs instilled locally, although systemic anti-tuberculous drugs are ineffective.

2.2 Severe Adverse Events

Systemic infection by BCG is a recognized but rare consequence of vaccination, and only seen in children with severe immune deficiencies such as Severe Combined Immune Deficiency, Chronic Granulomatous disease or Di George syndrome. Other rare adverse events include BCG osteitis and osteomyelitis (WHO, 1993; 1999; 2000, level 1).
3. VACCINE EFFICACY

BCG vaccine has high protective efficacy (approximately 80%) against meningeal and miliary tuberculosis in children. However, the protective efficacy against pulmonary disease is variable, ranging from 0% to 80%, with a lower degree of protection in tropical regions (American Academy of Pediatrics, 2000; WHO, 1999, level 1).

4. STORAGE AND ADMINISTRATION

BCG vaccine should be stored and transported at 2°C to 8°C. The diluents should not be frozen but kept cool. The vaccine must be kept refrigerated, and once the diluent has been added, used within 4 hours, and kept away from light (Academy of Medicine of Malaysia, 2001). Administration of BCG vaccine is through intra-dermal injection with a 25 or 26 gauge needle at the deltoid region of the upper arm, which will minimize post vaccination lymphadenopathy. Other less satisfactory techniques are percutaneous injections and use of jet injectors or bifurcated needles.

5. IMMUNISATION SCHEDULE

BCG is currently recommended at birth, or at first contact with health services. There is little scientific evidence on the efficacy of booster doses for BCG (WHO, 1993; 1999, level 1) [Grade A].

6. SPECIAL SITUATIONS

6.1 Premature and Low Birth Weight Babies
Infants less than 33 weeks are less likely to develop BCG scar and a reactive PPD tuberculin test after BCG vaccination. Premature babies thus need not be given BCG vaccine until they are at least 34 weeks, and with body weight more than 1800 g to 2000 g (Sedaghatian et al, 1998, level 8) [Grade C].

6.2 Babies born to HIV positive mothers
BCG should not be administered to children with symptomatic HIV infection. However, for babies born to HIV positive mothers, since the HIV status cannot be determined at birth, as none are likely to have symptoms of HIV infection, WHO recommends that they be administered BCG vaccine, especially in areas where the risk of tuberculosis is high (WHO, 1993; 1999, level 1) [Grade A]
DIPHTHERIA, TETANUS AND PERTUSSIS

1. INTRODUCTION

1.1 Diphtheria
Diphtheria is an acute infectious disease affecting the upper respiratory tract and occasionally the skin, vagina and conjunctiva. The clinical manifestations result from the action of an exotoxin produced by Corynebacterium diphtheriae. Diphtheria is acquired through personal contact, the incubation period being generally 2 to 5 days. It is a notifiable disease in Malaysia. There is a diminishing trend in incidence from 0.11 per 10,000 population in 1988 to 0.02 in 1998 (Ministry of Health Malaysia, 2002, level 1).

Diphtheria toxoid is produced by growing C. diphtheriae in a liquid medium, incubating the filtrate with formaldehyde to convert the toxin to toxoid, which is further purified and concentrated to achieve the necessary dosage. It is usually absorbed on to an adjuvant, either aluminium phosphate or aluminum hydroxide to increase the immunogenicity (Ministry of Health Malaysia, 2002, level 1; Academy of Medicine of Malaysia, 2001, level 8).

1.2 Tetanus
Tetanus is an acute disease caused by a highly potent neurotoxin (Tetanospasmin) produced by Clostridium tetani, which acts at the myoneural junction of skeletal muscle, and on neuronal membranes in the spinal cord, blocking inhibitory impulses to motor neurons. The disease is characterised by muscular rigidity with superimposed agonising contractions. The bacillus grows anaerobically at the site of wounds. Tetanus spores are present in the soil and may be introduced into the body during injury through puncture wounds, burns or trivial wounds. It is not spread from person to person, and the incubation period may vary from 2 days to 2 months, averaging about 10 days, although most cases occur within 14 days. Shorter incubation periods are said be associated with more heavily contaminated wounds, more severe disease and a worse prognosis. Death results from respiratory failure, hypotension, or cardiac arrhythmias (Ministry of Health Malaysia, 2002, level 1; American Academy of Pediatrics, 2000, level 1; Department of Health, United Kingdom, 1996, level 1; National Health & Medical Research Council, Australia, 1997, level 1).

Tetanus is a notifiable disease in Malaysia, with the reported incidence showing a general diminishing trend from 0.08 per 100,000 population in 1988 to 0.06 in 1998 (Ministry of Health Malaysia, 1999).
Tetanus vaccine is a toxoid extracted from the toxin through culture of C tetani. The cell free product is detoxified after treatment with formaldehyde, and usually adsorbed on to an adjuvant (either aluminium phosphate or aluminium hydroxide) to increase its immunogenicity (Ministry of Health Malaysia, 2002, level 1; Academy of Medicine of Malaysia, 2001, level 8).

1.3 Pertussis
Pertussis or ‘whooping cough’ is a highly contagious disease caused by Bordetella pertussis, an aerobic, gram-negative coccobacillus that invades the epithelium of the naso-pharynx, bronchi and bronchioles. Human transmission is through aerosol droplets. The asymptomatic incubation period is 7 to 10 days (ranging from 6 to 20 days), followed by the catarrhal stage of 2 to 7 days, and finally the paroxysmal cough stage lasting 1 to 8 weeks. A mild whooping cough syndrome can also be caused by other organisms, like Bordetella parapertussis and bronchiseptica, Mycoplasma pneumoniae, Chlamydia trachomatis and pneumoniae, and adenoviruses (Ministry of Health Malaysia, 2002 level 1; American Academy of Pediatrics, 2000, level 1).

Pertussis causes significant morbidity especially in those aged 3 months to 6 years. Mortality may be due to secondary bacterial pneumonia, hypoxia, encephalopathy or cerebral haemorrhage. Accurate figures on prevalence of pertussis in Malaysia are not available since it may be under-reported (Ministry of Health Malaysia, 2002, level 1).

For many years, the incidence of pertussis was controlled using combination vaccines containing whole-cell pertussis. However, concern about possible central nervous system adverse effects from this vaccine resulted in a drop in vaccination uptake and subsequent resurgence of the disease in many countries in the 1980’s and 1990’s. Consequently, many developed countries are currently using the acellular pertussis vaccine in their immunisation programme.

1.4 DTP Vaccine
Combination vaccines of diphtheria, tetanus, and pertussis toxoids are of two types - whole cell (DTP) and cellular vaccine (DTaP). DTP is the most widely used vaccine against pertussis. It consists of a suspension of whole-inactivated Bordetella pertussis bacteria combined with diphtheria and tetanus toxoids adsorbed on to an aluminium salt. DTaP contains one or more antigens derived from Bordetella pertussis with minimal or no endotoxin. The antigens include detoxified pertussis toxoid, filamentous hemagglutinin, agglutinogens and pertactin (Ministry of Health Malaysia HTA, 2002, level 1).
2. ADVERSE EFFECTS OF VACCINES

There has been much public concern on the adverse reactions to whole cell pertussis DTP vaccines, primarily focused on the whole cell pertussis component of the vaccine. The side effects include local, systemic, and anaphylaxis reactions. The frequent local reactions are erythema and induration with or without tenderness (Cody, 1981, level 4). A nodule may occasionally be present at the injection site for several weeks, while sterile abscesses have been reported to occur 6 to 10 times per one million doses of DTP (MMWR, 1991, level 1).

2.1 Systemic Reactions

Mild systemic reactions like fever, drowsiness, fretfulness, anorexia occurs frequently (Cody 1981 level 4). Fever usually occurs 24 hours or later after vaccination. However, if the fever persists for more than 24 hours, it should not be assumed to be due to DTP vaccination (MMWR, 1991, level 1; MMWR, 1996; level 1).

Moderate-to-severe systemic events occur infrequently and appear to be without sequelae. These include high fever (i.e. temperature greater than 40.5 °C), within 48 hours, unexplained by another cause; persistent, inconsolable crying lasting for 3 hours or more, within 48 hours of immunisation; collapse or shock-like episodes (hypotonic-hyposensitive episode) within 48 hours – occurring in 1 case to 1,750 doses administered (Cody, 1981, level 4), or short-lived convulsions (usually febrile) occurring within 3 days (Ministry of Health Malaysia, 2002, level 1; American Academy of Pediatrics, 2000, level 1).

There is consistent evidence of correlation between DTP vaccine and acute encephalopathy, although it has been insufficient to establish causality (Baraff, 1988, level 8; Miller, 1993, level 8; Cowan, 1993, level 8). Similarly, a causal relationship between DTP vaccine and permanent neurological damage has not been established (Cowan, 1993, level 1).

Immediate anaphylactic reactions such as breathlessness, hypotension and shock have been rarely reported after DTP vaccine, and there has been no death reported since the inception of vaccine-adverse-event reporting to CDC in 1978 (MMWR, 1991, level 1).

Severe reactions to vaccines containing diphtheria or tetanus antigens (DT) are extremely rare. An immediate anaphylactic reaction to tetanus and diphtheria toxoid containing vaccine (i.e DTaP, DT or DT) is a contraindication to further doses unless the patient can be desensitised to these toxoids, due to uncertainty as to which vaccine component (diphtheria, pertussis or tetanus) may be responsible. Persons who experience anaphylactic reactions may be referred to an allergist for
evaluation and possible desensitization (Ministry of Health Malaysia, 2002, level 1; American Academy of Pediatrics, 2000, level 1).

Overuse of tetanus toxoid can result in polynuclearphathy with an estimated incidence of 0.4 per million doses of tetanus toxoid (Ministry of Health Malaysia, 2002, level 1).

Despite some case reports, no increased risk of Guillain Barre Syndrome has been observed with the use of tetanus toxoid in whole cell or acellular pertussis vaccines (National Health & Medical Research Council, Australia, 1997, level 1). Hence, no special precautions are needed when immunising children with a history of Guillain Barre Syndrome (Ministry of Health Malaysia, 2002 level 1).

3. VACCINE EFFICACY

3.1 Diphtheria Vaccine

The most important factor of an age host response to immunity with diphtheria toxoid is the modifying effect of passively acquired maternal antibodies in young infants. This passive diphtheria antibodies seem to show a transient antibody response suppression to the second injection of DPT vaccine, although, there has been no response to the third injection of DPT vaccine (Ministry of Health Malaysia, 2002, level 1).

Primary immunisation with 3 doses of DTP vaccine stimulates the production of diphtheria antibody level in considerable excess of the minimum protective level (0.01 IU/ml). However, while natural immunity is life long, the duration of immunity after a primary immunisation series is variable. Studies on this issue have showed differing results, with duration of immunity ranging from 3-10 years. This could be due to differences in vaccines, vaccination schedules and levels of community exposure to Corynebacterium diphtheria (presence of natural boosting). In contrast, a booster dose at 2 years or at school entry (4-6 years) stimulates abundant production of diphtheria antitoxin with mean levels above 0.1 IU/ml. There is no defined level of antitoxin but it is believed that 0.01 IU/ml dose of Diphtheria is enough for clinical immunity against the disease, while a dose of 0.1 IU/ml may be needed for protection (Ministry of Health Malaysia, 2002, level 1).

The effectiveness of 3 or more doses ranged from 97 to 99.9% (Bisgard et al., 2000, level 9; Chen et al., 2000, level 9). Schoolchildren who received booster doses experienced protection against respiratory diphtheria (Bisgard et al., 2000, level 9). In Russia, it was also found that booster doses given at 6-8 years provided improved protection (Vitek et al., 1999, level 7). Thus, it is recommended that Diphtheria be
given as 3 primary doses with a booster a year after the primary doses, as well as another at 6-8 years of age.

3.2 Tetanus Toxoids Vaccine
Tetanus toxoid has an efficacy of more than 95%. Effective protection is provided by active immunisation, with complete primary immunisation (3 doses) conferring protection for at least 5 years. Immunity will last for at least 10 years after the 4th dose, and 20 years after the 5th dose (Ministry of Health Malaysia, 2002, level 1).

A tetanus antitoxin level of 0.01 IU/ml serum is considered as the minimum protective level (Chen, 1976, level 1). Case reports have shown that for patients with antitoxin level more than 0.01 IU/ml, the severity of tetanus was inversely proportional to the antitoxin level.

3.3 Pertussis Vaccine
The effectiveness of a 3-dose whole-cell pertussis vaccination was between 71 to 90% depending on the case definition used (De Serres, 1996, level 8). Acellular DTP with more than three component pertussis vaccines was found to be less efficacious than those with 2 or 3 whole-cell vaccines (Tinnion, 2000, level 1). Most studies measure pertussis antitoxin (FHA antibodies) and levels above 0.01 IU/ml are considered to be a response to the vaccine, affording a minimum protective level (Ministry of Health Malaysia, 2002, level 1).

4. STORAGE, DOSAGE AND ADMINISTRATION

4.1 Diphtheria Vaccine
Diphtheria vaccines should be stored at 2–8 °C. If the vaccine had been frozen, it should not be used (Ministry of Health Malaysia, 2002, level 1, Academy of Medicine of Malaysia, 2001, level 9). The recommended dose is 0.5 ml given intramuscularly (Ministry of Malaysia, 2002, level 1) [Grade A]

4.2 Tetanus Toxoid
Tetanus toxoid is stable and able to withstand room temperature for months (WHO, 1995 level 1). However, tetanus vaccine if part of DPT should be stored at 2-8 °C, and should not be frozen or exposed to light (Ministry of Health Malaysia, 2002, level 1; National Health & Medical Research Council, Australia, 1997, level 1; Department of Health, United Kingdom, 1996, level 1). The dose is 0.5 ml given intramuscularly. For primary immunisation, tetanus vaccines should not be given as a monocomponent vaccine, but combined with diphtheria (DT) and or pertussis (DPT) (Ministry of Health Malaysia, 2002, level 1; National Health & Medical Research Council, Australia, 1997, level 1) [Grade A]
4.3 Pertussis Vaccine

Pertussis vaccines should be stored at 2-8 °C and should not be frozen (Ministry of Health Malaysia, 2002, level 1; National Health & Medical Research Council, Australia, 1997, level 1; Department of Health, United Kingdom, 1996, level 1). The dose is 0.5 ml given intramuscularly at a 90° angle to the skin. The recommended site of injection is the anterolateral aspect of the thigh for infants, while for toddlers up to 4 years of age, the deltoid muscle is the recommended site (ACIP, 2002)) [Grade A]

5 ACCELERATED DTP IMMUNISATION SCHEDULE

The first dose of DTP at 3 months of age has been said to be too late to protect infants against pertussis (National Health & Medical Research Council, Australia, 1997, level 1; Bart, 1990, level 1). It has been shown that the first dose of DTP can be lowered to 6 weeks of age without compromising immunogenicity, for both the whole cell and acellular pertussis DTP vaccines (WHO, 1995, level 1; Bart, 1990, level 1; Ramsay, 1993, level 9; Edwards, 1995, level 1; Gustafsson, 1996, level 1). Booster doses of DTP at 12-24 months and at 4-6 years are recommended to maintain immunity against pertussis and diphtheria, where the national incidence has been successfully reduced (WHO, 1995 level 1; Bart, 1990, level 1; Frenkel, 1990, level 9; MMWR, 1991, level 1)) [Grade A]
POLIOVIRUS VACCINE

1. INTRODUCTION

Poliomyelitis is an acute viral infection ranging in severity from a non-specific illness to paralysis with permanent disability. About 90-95% of poliovirus infection is asymptomatic, while non-specific illness with low grade fever and sore throat occurs in 4-8% of infections. Aseptic meningitis with parasthesia occurs in 1-5% of patients a few days after the minor illness has resolved. Rapid onset of asymmetric acute flaccid paralysis with areflexia involving limbs occurs in 0.1% - 2% of infections, and residual paralytic disease involving the motor neurons (paralytic poliomyelitis) occurs in approximately 1 in 250 infections. Cranial nerve involvement and paralysis of respiratory muscles may also occur. Findings of mild pleocytosis and lymphocytic predominance in the cerebrospinal fluid (CSF) are characteristic of viral meningitis.

Adults who contracted paralytic poliomyelitis in childhood may develop the post-polio syndrome 30-40 years later, characterised by muscle pain, exacerbation of weakness, and/or new paralysis or weakness. This secondary illness resembling motor neuron disease, after an apparent silent period, is sometimes known as late post poliomyelitis muscular atrophy. Risk factors that may affect the potential for infection with poliovirus or the severity of clinical poliomyelitis include immune deficiency, injections, malnutrition, physical activity, pregnancy and tonsillectomy.

Four types of poliovirus vaccines are currently available - inactivated polio vaccine (IPV) of Salk, oral polio vaccine (OPV) of Sabin, enhanced-potency inactivated vaccine of Van Wezel (eIPV) and combinations with other vaccines like DTP-IPV. The vaccines are trivalent containing a mixture of the 3 strains of poliovirus.

2. ADVERSE EFFECTS

There have been many reports of Vaccine Associated Paralytic Poliomyelitis (VAPP) due to OPV, with an epidemiological study estimating the risk to be 1.3 cases per million vaccines. IPV does not cause VAPP and is currently recommended to prevent VAPP in a sequential regime. However, other studies have reported adverse events due to IPV like local reaction at injection site (43%), neurological disorders (12%), hypertension (10%) and allergic reactions (10%). Other rare but serious side effects like persistent crying, febrile seizures, apyretic seizures, uneasiness and shock have been reported (Ministry of Health Malaysia, 2002, level 1).
3. VACCINE EFFICACY

There is good evidence that OPV is efficacious. Children with diarrhoea receiving OPV should be re-immunised once the disease has resolved since it has been found that diarrhoea is a major factor in vaccine failure. The seroconversion rate for all types of poliovirus was found to be higher if an extra dose was given at birth in countries where poliomyelitis is still a problem. OPV is also found effective when given to preterm babies at 34-35 weeks of gestation (Ministry of Health Malaysia, 2002, level 1).

IPV was found to be as efficacious as OPV. It was also found that seroresponses to IPV were excellent and unaffected when combined with other vaccines in the same syringe. However, one study found that the immune response to pertussis was affected by combining DTP and IPV (Ministry of Health Malaysia, 2002, level 1).

Vaccines combining IPV with DTP are available. In addition, IPV or OPV can be given concurrently with many other vaccines like DTP, Hepatitis B, Hib, measles or MMR, and Varicella.

4. STORAGE, DOSAGE AND ROUTE OF ADMINISTRATION

The cold chain of polio vaccine should be maintained, and both OPV and IPV vaccines should be stored in the refrigerator at 4-10°C. OPV should be stored below 0°C. After thawing, it may be stored between 2-8 °C. IPV should be stored at 2-8°C.

The route of administration of OPV is by oral drops, while IPV is intramuscular, on the anterolateral aspect of the thigh or arm, or subcutaneously. Tetracoq (DPT-IPV) is administered intramuscularly as DTP vaccine is an adjuvant.

5. IMMUNISATION SCHEDULE

WHO recommends that 4 doses of OPV be given by 14 weeks of age, with a dose at birth in countries where poliomyelitis is still a problem. A 2-month interval is desirable between the first 2 doses to avoid interference with replication, the minimum interval in most circumstances being 6 weeks. The 3rd dose is recommended when the child is 6 - 18 months to complete the primary series, and a supplementary dose given before entering school i.e. at 4 - 6 years of age. For children not immunised in the first year of life, 2 doses of OPV should be given approximately 6 -8 weeks apart, followed by a third dose 2-12 months later. [Grade A]
For children immunised with IPV only, the primary series consists of 3 doses. The first 2 doses should be given at 1-2 month (4-8 weeks) intervals beginning at 2 months of age (minimum age 6 weeks) and a 3rd dose is recommended 6-12 months after the second dose. A supplemental dose of IPV should be given before the child enters school i.e. 4 - 6 years of age. [Grade A].

6. SPECIAL SITUATIONS

IPV is recommended in special cases like immuno-compromised patients such as HIV-infected and their household contacts, since OPV is contraindicated (Ministry of Health Malaysia, 2002, level 1) [Grade A]
HEPATITIS B VACCINE

1. INTRODUCTION

Hepatitis B (HB) is a major chronic viral illness worldwide with long-term complications of cirrhosis and hepatocellular carcinoma resulting in high mortality and morbidity. As the treatment is far from satisfactory, the best strategy is prevention. These include active immunisation with HB vaccine, avoidance of at-risk behaviour and possible sources of transmission, and strict adherence to universal precautions and good infection control procedures (Ministry of Health Malaysia, 2002, level 1).

Infants who become infected by perinatal transmission have a 90% risk of chronic infection and a 25% risk of dying of liver cancer. Furthermore, children younger than 5 years of age living with a person with hepatitis B infection can become infected via horizontal transmission and also have a higher likelihood of chronic infection and subsequent cirrhosis or cancer in early adulthood. In Malaysia, the incidence of HB has declined from 9.38 per 100,000 population in 1988 to 2.97 per 100,000 population in 1996. However, there are still about 1 million hepatitis B carriers in this country or about 5% of the population (Ministry of Health Malaysia, 2002, level 1).

HB immunisation provides adequate protection in the majority of recipients and prevents both vertical and horizontal transmission. The hepatitis B vaccine contains inactivated hepatitis B virus surface antigen (HbsAg) adsorbed onto aluminium hydroxide adjuvant. Several highly effective and safe hepatitis B vaccines produced by recombinant DNA technology are available. The original plasma-derived vaccine is no longer recommended (Ministry of Health Malaysia, 2002, level 1).

2. ADVERSE EFFECTS

Hepatitis B vaccine is generally safe and well tolerated. The most common adverse reactions are transient soreness and redness at injection site, low grade temperature, nausea, dizziness, malaise, rash, an influenza-like syndrome, arthritis, arthralgia and myalgia, that occur less frequently in infants and children than in adults. These symptoms resolve within 24-48 hours of vaccine administration, and the frequency of these reactions decrease with subsequent doses of the vaccine. Allergic reactions have been reported infrequently and anaphylaxis is very rare (Ministry of Health Malaysia, 2002, level 1).

Cases of Guillain-Barre syndrome, rheumatoid arthritis, demyelinating diseases of the central nervous system, and lichenoid reaction have been reported after hepatitis B immunisation. However, there is no
evidence of an association between vaccination and sudden infant death syndrome, multiple sclerosis, autoimmune disease or chronic fatigue syndrome (DeBiasa et al., 2002; American Academy of Pediatrics, 2000, level 1).

Thimerosal is a derivative of ethyl mercury and has been used as a preservative in vaccines since the 1930s for its efficacy in preventing bacterial contamination in opened, multi-dose containers. There is no convincing evidence of toxicity from doses of thimerosal used in vaccines (McPhillips & Marcuse, 2001, level 2).

3. VACCINE EFFICACY

High seroconversion rates and protective concentrations of anti-Hbs (≥10mIU/ml) are achieved when hepatitis B vaccine is administered in any of the various 3-dose schedules, including those begun soon after birth in term infants. The use of a 3-dose regimen has been shown to be highly efficacious. The vaccine is effective in preventing HB infection in individuals who produce specific anti-Hbs (Ministry of Health Malaysia, 2002, level 1). The immune response using 1 or 2 doses of a vaccine produced by one manufacturer followed by 1 or 2 more subsequent doses from a different manufacturer had been demonstrated to be comparable to a full course of immunisation with a single product. For children with normal immune status, routine booster doses of vaccine are not recommended (American Academy of Pediatrics, 2000, level 1).

4. STORAGE, DOSAGE AND ADMINISTRATION

The vaccine should be stored at 2 to 8 °C. Freezing will destroy its potency. The vaccine is a white, slightly opalescent liquid. Any visible change in the product, such as precipitates, may indicate incorrect storage conditions and consequent reduction in immunogenicity. Such vaccines should be discarded. The dose of vaccine is 0.5 ml, administered intramuscularly in the antero-lateral thigh for neonates and infants, and the deltoid area for children. Administration intradermally or in the buttocks has resulted in poor immune response, and is thus not recommended. Simultaneous administration with other vaccines at different sites is safe and efficacious (Ministry of Health Malaysia, 2002, level 1; DeBiasa et al., 2002, level 1). In patients with a bleeding diathesis, the risk of bleeding after intramuscular vaccine infection can be minimized by administration immediately after the patient receives replacement factor, use of a 23-gauge needle or smaller, and application of direct pressure to the immunisation site for at least 2 minutes (American Academy of Pediatrics, 2000, level 1) [Grade A]
5. **SPECIAL SITUATIONS**

5.1. **Infants Born to HbsAg-Positive Mothers**
Infants born to HbsAg-positive mothers should be cleansed of blood in the delivery room. Both hepatitis B vaccine and HBIG (0.5ml intramuscularly) should be given simultaneously at different sites as soon as possible, preferably within 12 hours after birth. Subsequent doses of hepatitis B vaccine should be given as recommended.

5.2. **Preterm Infants**
For preterm infants who weigh less than 2 kg at birth, the initial vaccine dose should not be counted in the required 3-dose schedule. Thus, a total of 4 doses are recommended in this circumstance. These infants should be tested serologically for anti-HBs and HbsAg 1 to 3 months after completion of the immunisation series. Infants with anti-HBs concentrations of less than 10mlU/ml and who are HbsAg-negative should receive 3 additional doses of vaccine at 0, 1 and 6 months followed by testing for anti-HBs 1 month after the third dose (DeBiasa et al., 2002, American Academy of Pediatrics, 2000, level 1). [Grade A]

5.3. **Serologic Testing**
Susceptibility testing before immunisation is not indicated routinely for children or adolescents. Routine post-immunisation testing for anti-HBs is also not necessary. However, testing is advised 1 to 2 months after the third vaccine dose for patients on hemodialysis, persons with HIV infection, those at occupational risk of exposure from sharps injuries, immunocompromised patients at risk of exposure to HBV, regular sexual contacts of HbsAg-positive persons, and infants born to HbsAg-positive mothers (American Academy of Pediatrics, 2000, level 1 ). [Grade A]
HAEMOPHILUS INFLUENZAE VACCINE

1. INTRODUCTION

*Haemophilus influenzae* is a respiratory pathogen of humans causing infections ranging from asymptomatic colonization of the upper respiratory tract to serious invasive disease. It is an important pathogen in children causing considerable morbidity, mortality and health care expense, both worldwide and locally (Ministry of Health Malaysia, 2002, *level 1*).

Invasive disease is associated with encapsulated strains of the organism. There are six capsular serotypes, designated a-f, the majority of invasive diseases being caused by *Haemophilus influenzae* type B. Meningitis is the most common invasive Hemophilus influenza type B (Hib) infection. Most cases of Hib meningitis in Malaysia occur in children under 12 months old, and it is rarely encountered in those under 3 months and beyond 5 years of age (Ministry of Health Malaysia, 2002, *level 1*).

The Hib vaccines available presently consist of polyribosylribitol phosphate (PRP) chemically linked (conjugated) to a variety of carrier proteins. This carrier protein ensures a good antibody response to the Hib capsular polysaccharide. Four types of vaccine are available – PRP-outer membrane protein conjugate vaccine (PRP-OMP), PRP-tetanus toxoid conjugate (PRP-T), PRP-Hib oligosaccharide conjugated vaccine (PRP-HbOC) and PRP-diphtheria toxoid conjugate vaccine (PRP-D) - of which only the first are currently available in Malaysia (Ministry of Health Malaysia, 2002, *level 1*).

2. ADVERSE EFFECTS

Adverse reactions to Hib conjugate vaccines are few, mostly pain, redness, and swelling at infection site, occurring in about 5-25% of recipients. These symptoms are mild and last for less than 24 hours. Systemic reactions such as fever and irritability are infrequent (Ministry of Health Malaysia, 2002, *level 1*).

The combination vaccine (DTwP +Hib) is well tolerated by infants and no significant side-effects have been reported (Ministry of Health Malaysia, 2002, *level 1*; Hussey, 2002; Cherian, 2002; Araujo, 2000). The local reactions reported were mainly transient pain, redness, induration and some low-grade fever (Lolekha, 2001). No vaccine-related serious adverse events have occurred when (DTaP-IPV) and Hib vaccine are used, either when mixed in the same syringe or given separately (Knutsson, 2001). A lower incidence of adverse events has
been reported following the Hib+DTaP combination vaccine compared to the Hib+DTwP (Gylca, 2000, level 8).

3. VACCINE EFFICACY

The protective superiority of any one of the three vaccines - PRP-T, PRP-OMP and HbOC - has not been demonstrated, and efficacy studies indicate that these vaccines are suitable for prevention of Hib disease in infants and children. In randomized controlled trials, antibody response to some vaccines was higher after the first dose, but the levels were not significantly different after 3 doses (Ministry of Health Malaysia, 2002, level 1).

4. COMBINATION OF VACCINES

Effective immunisation of children against multiple disease is best tackled by giving several antigens in one injection. The preparation of the single injection could be done either during manufacture of vaccines or immediately before administration (Ministry of Health Malaysia, 2002 level 1). DTwP mixed with PRP-T and given concurrently with OPV, PRP-T mixed with DTwP, DTPw-IPV mixed with Hib and separate HBV achieved satisfactory antibody production against PRP (Araujo, 2000; Ministry of Health Malaysia, 2002, level 1). There was no interference to any of the components when OPV, DTaP and Hib vaccine were given separately or when DTaP was mixed with Hib and given with OPV (Rennels et al, 2000, level 2).

5. STORAGE, DOSAGE AND ROUTE OF ADMINISTRATION

Conjugate vaccines should be stored at 2-8°C, and must not be frozen. Each dose of conjugate vaccine is 0.5ml and given intramuscularly. The use of fractional dose regimens showed adequate serological response and immunological memory (Ministry of Health Malaysia, 2002. level 1; Fernandez, 2000). [Grade A]

6. SCHEDULE

There is good evidence that immunisation with three doses of PRP-T vaccine at 2, 3, 4 or 2, 4, 6 months is highly immunogenic (Ministry of Health Malaysia, 2002 level 1) [ Grade A]

The high efficacy of PRP-T given in infancy and virtual disappearance of the disease in the UK, suggest that the booster dose may not be required for a population where high vaccination coverage (>90%) is achieved (Ministry of Health Malaysia, 2002; level 1; Health, 2002). [Grade A]
A single Hib vaccine dose is efficacious in preventing Hib invasive disease in children between the ages of 1-4 years. The need for catch-up should always be considered when introducing Hib vaccine in routine immunisation programs (Gallo, 2002). [Grade A]

7. SPECIAL SITUATIONS

7.1 Premature Babies
Although most immature infants may show an inadequate antibody response to the initial immunisation, many pre-term infants benefit from vaccination when immunisation is commenced at the same chronological age as term infants (Kristensen, 1996; American Academy of Pediatrics, 2000, level 1). [Grade A]

7.2 Thalassaemia and Splenectomy
Hib conjugate vaccine is immunogenic in patients with Thalassemia major irrespective of whether or not a splenectomy had been performed. However, the need as well as the timing of booster vaccination to maintain long-term immunity has to be assessed (Cimaz, 2001; level 9; Kristensen, 1994, level 8; Ambrosino, 1992, level 8). [Grade C]

7.3 HIV Infection
The effectiveness of the Hib conjugated vaccine has been found to be reduced in HIV infected infants (Read, 1998, level 8; Gibb, 1995, 1996, level 8; Rutstein, 1996, level 8; Peters, 1996, level 9, Madhi, 2002, level 8). They were found to have titer below the protective level at 1 year, and thus, the need for re-immunisation of children with HIV infection against Hib requires further evaluation (Gibb, 1996, level 8). [Grade C]
MEASLES, MUMPS AND RUBELLA VACCINE

1. INTRODUCTION

1.1 Measles
Measles is a highly infectious viral (RNA) disease and a major health issue. It affects almost the entire population in the absence of an immunisation programme. Measles is transmitted primarily by respiratory droplets from person to person. Primary viraemia occurs 2-4 days following exposure with an intense secondary viraemia occurring 3-4 days later. Community studies in developing countries have documented case fatality rates of up to 3-15%. The mortality is highest in children under 2 years of age, those who are malnourished, and living in crowded conditions (Ministry of Health Malaysia, 2002, level 1).

Measles vaccine is a live attenuated vaccine cultured in chick embryo cells. The vaccine contains a stabiliser that makes it more heat resistant. However, after reconstitution, at 22 ºC to 25 ºC it will lose 50% of its potency, while it becomes completely inactivated in 1 hour at temperatures of over 37ºC.

The efficacy of measles vaccine is 95% for persons vaccinated at 12 months, and 98% for those vaccinated at 15 months of age. A local evaluation of vaccine efficacy showed seroconversion rates ranging from 93.7-98.9% for children aged 9-24 months, with rates being better for those aged 11-24 months (96.4-98.9%) than those who were 9-10 months old (93.7-95.3%) (Ministry of Health Malaysia, 2002, level 1).

The majority of vaccinated individuals appear to develop life long immunity, but waning vaccine- induced immunity does exist (secondary vaccine failure). However, the measles that occurs in immunised persons has been reported to be milder than in those who were not immunised. There is a minimum primary vaccine failure rate of 2-5%, which could be higher if the vaccine were given before 12 months of age (Ministry of Health Malaysia, 2002, level 1).

1.2 Mumps
Mumps is a paramyxovirus infection. It occurs primarily in children, with a peak incidence at 5-9 years of age. Complications include pancreatitis, oophoritis, orchitis (unilateral orchitis has been reported in up to 20% post-pubertal males with clinical mumps, although sterility is rare), hepatitis, myocarditis and thyroiditis. Benign meningeal signs appear in up to 15% of cases, but permanent sequelae is rare. A serious rare complication is unilateral nerve deafness.
Mumps vaccine is a live attenuated vaccine prepared in chick embryo cell cultures. The most widely used strain at present is Jeryl Lynn B (Bakshi et al., 1990), while the other strains available are Rubini and Urabe. The Urabe strain was withdrawn in 1992 after an association with increased risk of aseptic meningitis was reported in other countries (Furesz, 1990), while the Rubini strain has been shown to be associated with primary vaccine failure (Schlegel, 1999). Seroconversion after a single dose of mumps vaccine was reported to range from 90-100%. The duration of vaccine induced immunity is unknown (antibodies have been shown to persist for 9.5 years after MMR administration) but epidemiological and serological data over the past 30 years indicate the persistence of antibodies and continuing protection against infection. It is anticipated that a two dose MMR policy will effectively deal with most cases of primary vaccine failure that have a risk of mumps in later life (Ministry of Health Malaysia, 2002, level 1).

1.3 Rubella

Rubella is an RNA virus belonging to the Togaviridae group of viruses. It is transmitted through droplet spread, while congenital infection occurs as a result of viraemia during pregnancy. The teratogenic effects are produced as a result of an inflammatory response to the virus, and depressed mitosis, resulting in hypoplasia in the developing foetus. Rubella associated defects occur in 100% of pregnancies if infection occurs in the first 11 weeks, 50% in infections at 11-12 weeks and 35% in 13-16 weeks. The common permanent manifestations of congenital rubella include sensorineural deafness, mental retardation, cataracts, congenital heart defect, retinopathy, spastic diplegia, growth retardation, hepatosplenomegaly, thrombocytopenia and meningoencephalitis.

Rubella vaccine is a freeze-dried preparation that is stored at 2-8°C, and when reconstituted with diluent fluid, is given in a dose of 0.5 mL subcutaneously. A serum antibody to rubella is induced in at least 95% of recipients following a single dose at 12 months of age or later. Vaccine induced antibody has been shown to persist for at least 16 years and protection against clinical rubella appears to be long term. However primary vaccine failures do occur and antibody levels can wane (Ministry of Health, 2002, level 1).

1.4 MMR Vaccine

The MMR vaccine is a freeze-dried preparation containing live attenuated measles, mumps and rubella viruses.
2. ADVERSE EFFECTS OF MMR

There are minimal adverse reactions following vaccination with MMR including local pain, local induration, malaise, fever or a rash that usually occurs a week after immunisation, lasting for 2-3 days. Potentially serious complications include Idiopathic Thrombocytopenic Purpura (ITP) (3.3 per 100,000), arthropathy, febrile convulsions, urticaria (0.6 per 10 000) and parotid swelling. However, the mumps component of the MMR vaccine is known to be associated with meningitis at an estimated rate of 1 in 50,000 to 1 in 1 million doses, which is far less common than with the natural illness (10-15%) (Ministry of Health Malaysia, 2002, level 1).

The current evidence only establishes a causal relation between MMR vaccination and anaphylaxis, thrombocytopenia, febrile seizures, and acute arthritis. However, no causal link has been established linking MMR to autism and inflammatory bowel diseases (Ministry of Health Malaysia, 2002, level 1; Madsen et al, 2002; Taylor et al, 2002). The general contraindications to MMR vaccine are as for all live vaccines (Ministry of Health Malaysia, 2002, Level 1). Although no anaphylactic death associated with administration of MMR vaccine has been reported, this adverse event can be life threatening. Adrenaline should be available for immediate use at any site where vaccines are administered in case symptoms of anaphylaxis occur (ACIP, 1998; American Academy of Pediatrics, 2000, Patja, 2000).

Children with allergy to eggs can safely receive MMR vaccine since the rare, serious allergic reactions after MMR are believed to be caused not by egg antigens, but by other components of the vaccine (e.g. MMR, its component vaccines, and other vaccines contain hydrolyzed gelatin as a stabilizer) (Ministry of Health Malaysia, 2002, level 1).

3. VACCINE EFFICACY

The vaccine is highly immunogenic with seroconversion rates of 96-100% for measles, 90-100% for mumps and 99-100% for rubella. Protection conferred by a single dose given after 12 months of age is long lasting in the majority of persons. However between 5-10% of vaccinated individuals may either have primary vaccine failure or lose protection, while 99% of individuals who receive two doses (separated by at least 4 weeks) after 12 months of age have long lasting immunity to measles (Ministry of Health Malaysia, 2002, level 1). There is conflicting evidence on the efficacy of MMR vaccination under 12 months of age. There has been a suggestion that as immunisation rates improve, maternal antibodies may wane sooner in mothers who received immunisation rather than the natural disease, hence allowing
for a lower minimum age for measles and other immunisation (Ministry of Health Malaysia, 2002, level 1).

4. STORAGE, DOSAGE AND ROUTE OF ADMINISTRATION

MMR vaccine should be stored at 2°C to 8°C and must be protected from ultraviolet light. Reconstituted measles vaccine is very unstable and quickly loses potency at room temperature after reconstitution, and hence should be discarded if not used within 8 hours even if stored in a refrigerator (ACIP, 1998). The dosage is 0.5 ml given by intramuscular or deep subcutaneous injection (Department of Health, United Kingdom, 1996). [Grade C].

5. SCHEDULE

A 2-dose MMR is recommended to be given at 12 months and at school entry (6 to 7 years). However, for Sabah, it is recommended that monovalent measles vaccine be given to children at 6 months of age, followed by MMR at 12 months and at school entry (6 to 7 years) (WHO/ACIP 1998). [Grade A]

6. SPECIAL SITUATIONS

6.1. Measles Immunisation in HIV Infected Children:
HIV-infected children, adolescents, and young adults without evidence of severe immuno-suppression should receive MMR vaccine. The first dose should be administered at 12 months of age. The second dose may be given as early as 28 days after the first dose. In the event of an outbreak in the community, vaccination with mono-valent measles vaccine (or MMR) is recommended for infants as young as 6 months when exposure to natural measles is considered likely. Children vaccinated before the first birthday should be revaccinated with MMR at 12 months, and an additional dose may be given 28 days later (AAP, 1999) [Grade A]

6.2. Steroid Treatment
Patient who received steroids at a dose equivalent to or greater than a prednisone dose of 2 mg/kg of body weight per day, or a total of 20 mg per day, or on alternate days for an interval of 14 days or longer, should avoid vaccination with MMR and its component vaccines for at least 1 month after cessation of steroid therapy. Similarly, those receiving prolonged or extensive topical, aerosol, or other local corticosteroid therapy that causes clinical or laboratory evidence of systemic immuno-suppression, should also avoid vaccination with MMR for at least 1 month after cessation of therapy. Such persons can generally receive MMR, or its component vaccines, immediately after cessation of
treatment, although some prefer waiting until 2 weeks after completion of therapy. MMR, or its component vaccines, should not generally be administered to persons who have a disease that suppresses the immune response, or those who are receiving either systemic or locally administered corticosteroids (ACIP 1998). [Grade A]

Recent evidence indicates that high doses of immunoglobulins can inhibit the immune response to measles and rubella vaccine for 3 months or more, and hence, MMR immunisation should be delayed (ACIP 1998). [Grade A]
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