WORLD HEALTH ORGANIZATION | **ORGANISATION MONDIALE DE LA SANTE**

REGIONAL OFFICE FOR THE WESTERN PACIFIC
BUREAU REGIONAL DU PACIFIQUE OCCIDENTAL

REGIONAL COMMITTEE WPR/RC54/5

Fifty-fourth session 22 July 2003
Manila, Philippines
8-12 September 2003 ORIGINAL: ENGLISH

Provisional agenda item 11

EXPANDED PROGRAMME ON IMMUNIZATION: MEASLES AND HEPATITIS B

To build on the Region's achievement of poliomyelitis-free status, certified on 29 October 2000, two new pillars to strengthen the Expanded Programme on Immunization have been proposed by international experts and by the Technical Advisory Group on the Expanded Programme on Immunization and Poliomyelitis Eradication (TAG): measles elimination and hepatitis B control.

Immunization in the Region has already reduced measles cases by 90% and measles deaths by 95% compared with the pre-vaccine era. However, measles remains the leading vaccine-preventable cause of child deaths in the Region. Improved use of a safe, effective, and inexpensive vaccine could prevent these deaths. There is now a global and regional scientific consensus that regional measles elimination is technically feasible.

Unlike other EPI diseases, the main burden of hepatitis B is in adults. Protecting infants against hepatitis B infection will prevent an important disease burden in later life. The Western Pacific Region suffers disproportionately from this disease; in 2000 it was estimated that over half of the global disease burden was in the Western Pacific Region, which contains only a quarter of the global population. Every country and area in the Region now includes hepatitis B vaccine in its immunization programme. However, more work is needed to make sure that every infant who is born is protected from hepatitis B infection. Hepatitis B control makes a good partner for measles elimination, as control of hepatitis B requires strengthening of routine immunization services.

The Regional Committee is asked to discuss and endorse the selection of measles and hepatitis B control as two new pillars to strengthen the EPI.

1. CURRENT SITUATION

The Expanded Programme on Immunization (EPI) was established by the World Health Assembly in 1974[1] and was designed to build upon the success of smallpox eradication. Since then the EPI has been progressively established in countries of the Region and is now a fundamental part of the health sector in all countries. WHO works closely with a number of partners to implement the EPI, notably the United Nations Children's Fund (UNICEF) within the United Nations system, bilateral donors, and the Global Alliance on Vaccines and Immunization (GAVI) and Rotary International, from the nongovernmental sector.

In 1988, the Forty-first World Health Assembly resolved to eradicate poliomyelitis by the year 2000[2] and the Regional Committee, at its thirty-ninth session, resolved to eradicate it from the Region by 1995.[3] Poliomyelitis eradication in the Western Pacific Region was an effective way of strengthening the EPI in the Region and the Western Pacific was the second WHO region (after the Region of the Americas) to achieve poliomyelitis-free status.

Although the poliomyelitis-free status of the Region was certified in 2000, the full potential gains from immunization have not yet been obtained. For example, of the more than 25.3 million children estimated to have been born in the Region in 2002, more than 5 million did not receive the recommended three doses of diphtheria-tetanus-pertussis vaccine (DTP) and 4.9 million did not receive measles vaccine. Hepatitis B vaccine coverage was only 68.1% (compared with 80.1% for DTP in 2001).

A detailed discussion of the recent work of the Expanded Programme on Immunization in the Region can be found in *The work of WHO in the Western Pacific Region: 1 July 2002-30 June 2003* (pp. 3-15).

[1] Resolution WHA27.57.
[2] Resolution WHA41.28.
[3] Resolution WPR/RC39.R15.

1.1 Measles

Measles remains a leading cause of disease, disability, and death among children in the Region. Of the global total of deaths among children, about 11% are due to measles (compared with 8% from AIDS and 4% from malnutrition). The measles virus is circulating in in Cambodia, some provinces of China, Japan, the Lao People's Democratic Republic, Malaysia, Papua New Guinea, the Philippines and Viet Nam. Some countries have achieved elimination, although this has not always been maintained (measles has, for example, re-emerged in Mongolia).

In May 2003, the Fifty-sixth World Health Assembly adopted a resolution to reduce global measles mortality (Annex 1).[4]

1.2 Hepatitis B

Every day, about 800 people die from hepatitis B infection in the Region. However, most of these deaths are not recognized as being due to hepatitis B as most occur in adult life as a result of liver cancer and cirrhosis that develop many years after infection. Hepatitis B vaccine is the first anticancer vaccine. It is a relatively recent addition to the EPI but is now included in the immunization programme of every country in the Region. The Western Pacific is the first WHO region to achieve this. However, more work is needed to increase coverage with hepatitis B vaccine and thereby prevent more infections.

1.3 Regional plans for measles elimination and hepatitis B control

Regional plans have been prepared for both measles elimination and hepatitis B control (Annexes 2 and 3). These plans were proposed by two separate expert meetings in April 2002 (for measles) and June 2002 (for hepatitis B). Both plans were then reviewed by the Technical Advisory Group on the Expanded Programme on Immunization and Poliomyelitis Eradication (TAG) in November 2002.

[4] Resolution WHA56.20.

2. ISSUES

2.1 Measles

Measles control is at different stages across the Region. While most countries are ready to move towards elimination, the expert group considered that it was premature to set a date for regional elimination, although it considered that measles elimination was the only rational goal for measles control. The target date for elimination will therefore be established through a process of annual reviews.

The global and regional scientific consensus is that measles elimination is technically feasible, but requires a high level of political commitment and sufficient financing.

To achieve measles elimination, some Member States will need to undertake additional activities including increasing routine coverage, delivering a second opportunity for measles immunization, enhanced disease surveillance, and laboratory confirmation of suspected measles cases.

2.2 Hepatitis B

In contrast to measles elimination, hepatitis B control is essentially achieved by strengthening routine immunization services through the delivery of three doses of vaccine, particularly a timely birth dose, to prevent perinatal transmission.

2.3 Surveillance

As with poliomyelitis, monitoring of measles control activities will be primarily through disease surveillance. For hepatitis B, the primary method of monitoring will be through routine coverage data – an improvement in the quality of routinely reported coverage data will therefore be required in many countries.

3. ACTIONS PROPOSED

The Regional Committee is asked to:

(1) endorse the selection of measles elimination and hepatitis B control as the two new pillars to strengthen the Expanded Programme on Immunization;

(2) confirm that measles elimination should be a regional goal;

(3) agree that the target date for regional measles elimination should be based on an annual review of progress;

(4) confirm that the objective of hepatitis B control programmes should be HBsAG prevalence of less than 1% in five-year-olds born after immunization started.

The following actions by Member States are proposed for consideration by the Regional Committee:

Measles

(1) offer all children a second opportunity[5] for measles immunization;

(2) improve measles surveillance systems by ensuring laboratory confirmation of suspected measles cases;

Hepatitis B

(1) improve the quality of routinely reported immunization coverage data and monitor these data, together with disease data, at district level in order to improve programme management;

(2) add receipt of three doses of hepatitis B vaccine by the age of 12 months to the definition of a "fully immunized child" and monitor the delivery of a scheduled birth dose of hepatitis B vaccine within 24 hours of birth;

[5] A "second opportunity" is a strategy to provide a first dose for children who were missed in the initial immunization round and a second dose to those who received a first dose (to protect the small proportion not protected by a single dose).

(3) ensure that coverage with hepatitis B vaccine is as high as with DTP and that there is coverage of at least 80% (ideally 95%) of each birth cohort and in every district.

ANNEX 1

FIFTY-SIXTH WORLD HEALTH ASSEMBLY **WHA56.20**

Agenda item 14.7 **28 May 2003**

Reducing global measles mortality

The Fifty-sixth World Health Assembly,

Alarmed by the unacceptable burden of nearly 800 000 measles deaths annually, occurring mostly in infants and young children living in developing countries;

Recognizing that the current disease burden of measles is the result of underutilization of measles vaccine caused by inadequately supported immunization programmes and disease surveillance systems;

Stressing the importance of achieving the goal adopted by the United Nations General Assembly special session on children (2002) to reduce deaths due to measles by half by 2005, compared with the 1999 level, and the target contained in the United Nations Millennium Declaration to reduce the under-five child mortality rate by two-thirds by the year 2015;

Recognizing the availability of safe, effective and inexpensive measles vaccines and proven strategies to reduce measles mortality;

Welcoming the remarkable progress that has been made by the Measles Initiative partnership to reduce measles deaths in Africa;

Noting the critical importance of routine immunization services as the foundation of a strategy to reduce measles deaths in a sustainable manner, and the essential role of integrated epidemiological and laboratory surveillance for measles in guiding control efforts;

Having considered the report on the strategy for child and adolescent health and development, which identifies measles as one of the five preventable communicable diseases that account for the vast majority of childhood deaths,

1. URGES Member States:

(1) to implement fully the WHO-UNICEF strategic plan for measles mortality reduction 2001-2005 in countries with high measles mortality within their national immunization programmes;

Annex 1

(2) to provide the financial support necessary for full implementation of national immunization programmes in which the strategy to reduce measles mortality is embedded, including measles vaccine for routine and supplementary immunization activities and strengthening of epidemiological and laboratory surveillance for measles and other vaccine-preventable diseases;

(3) to use the strategic approach of reducing global measles mortality as a tool for strengthening national immunization programmes, with special emphasis on improving access to immunization services, ensuring safe immunization practices, and enhancing human-resource capability, laboratory networks, epidemiological surveillance and cold-chain systems;

2. REQUESTS the Director-General:

(1) to work with Member States through regional offices to strengthen national immunization programmes and disease-surveillance systems, using the status of measles control as one of the leading indicators of progress in reducing child mortality;

(2) to strengthen partnerships at global, regional and subregional levels with UNICEF and other international bodies, nongovernmental organizations and the private sector to mobilize the additional resources needed to implement fully the WHO-UNICEF strategy for the expanded programme on immunization and measles mortality-reduction strategies;

(3) to report to the Fifty-seventh World Health Assembly, through the Executive Board, on progress made in implementing this resolution.

Tenth plenary meeting, 28 May 2003
A56/VR/10

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WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR THE WESTERN PACIFIC

WESTERN PACIFIC REGIONAL PLAN OF ACTION FOR MEASLES ELIMINATION

Manila, Philippines
January 2003

(WP)ICP/EPI/5.2/001-E English only

WESTERN PACIFIC REGIONAL PLAN OF ACTION FOR MEASLES ELIMINATION

The Regional goal is to eliminate measles, with a target date to be established through an annual review process.

Not for sale

Printed and distributed by

World Health Organization
Regional Office for the Western Pacific
Manila, Philippines

January 2003

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EXECUTIVE SUMMARY

Measles remains the leading cause of vaccine-preventable death and disability among children in the Western Pacific Region. Following certification of polio-free status in 2000, it is now time to direct attention to the elimination of this killer disease.

Central to this Regional Plan is a strategy for providing a second opportunity for measles immunization. A single dose of measles vaccine protects about only 85% of children, but 95% of the population must be immune to stop transmission. A second dose, given after the age of one year, will protect 99% of children. Therefore, to eliminate measles, children must have a second opportunity that reaches practically every child.

The plan describes objectives in three strategic areas, which are directed at producing, sustaining and verifying interruption of virus transmission:

- ✓ immunization;
- ✓ surveillance; and
- ✓ laboratory support.

The immunization objectives are to strengthen routine immunization and to provide a second opportunity for measles immunization. The surveillance objectives are to progress from aggregated data reporting to a full case-based system as incidence levels fall and to integrate measles surveillance with existing active acute flaccid paralysis (AFP) surveillance. The laboratory support objectives are to establish national accredited measles laboratories as part of a Regional laboratory network to confirm clinical diagnosis and identify the source of viruses. In addition, in a number of countries in the Region with inadequate measles control, further efforts will be needed to improve measles case management, including use of vitamin A in order to reduce measles-associated mortality and disability.

As the countries of the Region are in very different stages of and have different capacities for measles control, no Regional target date for elimination has been set. It is proposed that this date will be established through an annual review of progress in measles control in the Region.

GLOSSARY OF TERMS

Measles control: Reduction of measles morbidity and mortality in accordance with targets; continued intervention measures are required to maintain the reduction.

Measles elimination: The situation in a large geographical area in which endemic transmission of measles cannot occur and sustained transmission does not occur following the occurrence of an imported case; continued intervention measures are required.

Measles eradication: Interruption of measles transmission worldwide as a result of deliberate efforts; intervention methods may no longer be needed. Eradication represents the sum of successful elimination efforts in all countries.

Routine immunization: The regular provision of immunizations to successive birth cohorts of children at fixed sites or by outreach activities.

Mass immunizations. A campaign that targets all children of a specified age (usually wider age range than for routine immunization) that are in the target area (usually national).

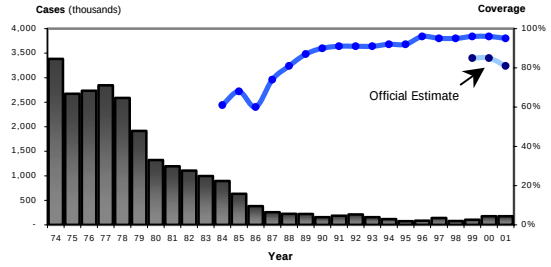
Second opportunity: A strategy to provide a first dose for children who were missed by the initial opportunity and a second dose to those who did receive a previous dose (to protect the small proportion not protected by a single dose).

WESTERN PACIFIC REGIONAL PLAN OF ACTION FOR MEASLES

1 BACKGROUND

About 40 years ago, a vaccine was invented against measles. Safe, effective and cheap, it had the potential to wipe out a disease that has killed children for centuries. Yet, measles remains the leading cause of vaccine-preventable death among children, estimated at over 30 million cases and 875 000 deaths in 1999. Although measles immunization programs have produced impressive results, achieving an estimated 75% reduction in cases globally and a 95% reduction in cases in the Western Pacific, there are still an estimated 1 170 000 cases and 32 000 deaths in the Region (See Figure 1 for reported cases and immunization coverage). These cases, and the resulting disability and deaths, are preventable.

Figure 1. Regional Reported Measles Cases and Measles Vaccine Coverage, Western Pacific Region, 1974-2001



Note: China officially adopted the best estimate method in 1999 as the administrative method underestimated births. Both best estimate and administrative methods for estimating coverage have been reported for years 1999-2001. (Because China accounts for most births in the Region, the change in reporting in China affected the Regional coverage significantly).

The countries of the Region have achieved polio-free status (certified on 29 October 2000). Now it is the time to add to this achievement and eliminate measles from the Western Pacific Region by building on the control efforts to date (Annex 1) and by using the strategies in the Global Measles Mortality Reduction and Regional Elimination Strategic Plan (2001-2005).

A second opportunity for measles immunization is a critical success factor in achieving elimination.

2 RATIONALE

Until it is eliminated, measles will continue to cause large epidemics, which are costly in terms of loss of life, disability and health resources, which are diverted to control outbreaks. On average, in a non-immune population, one child with measles will infect nearly 20 others. If, on the other hand, at least 95% (19 of 20) are immune to measles, transmission of the virus is effectively interrupted. Each child would, on average, pass the infection to just less than one child, leading to eventual elimination of measles. Therefore, to eliminate measles, it is necessary to achieve ~95% population immunity.

Measles elimination is achieved when population immunity is high enough to interrupt indigenous transmission, and an importation leads to only a limited outbreak. Measles elimination does not mean zero cases because importations and limited secondary transmission are likely to occur. The extent of spread from an importation is an indicator of population immunity. Mathematical modelling suggests that if population immunity is close to the threshold level needed to maintain elimination, an importation is likely to cause an outbreak of less than about 50 cases.

Measles immunization at age nine months protects about 85%; a second dose, given after age 12 months protects 99% of children. Therefore, with even 100% coverage of a single dose the ~95% population immunity for elimination cannot be achieved, but with very high coverage of two doses it can. The second opportunity achieves two important outcomes:

1. Children who missed the first dose are given one, essential to achieve the population immunity threshold; and
2. Children who received the first dose but are in the ~15% who did not seroconvert are given a second dose that will then protect practically all of

these 'vaccine failures' to achieve the population immunity threshold.

Goal:
To eliminate measles from the Region, with a target date to be established through an annual review process.

3. REGIONAL OBJECTIVES

The following Regional objectives are proposed to monitor progress towards the elimination goal:

- ✓ to annually review Regional progress to establish the target date for Regional measles elimination;
- ✓ to achieve and maintain the interruption of measles transmission in countries with an existing elimination goal;
- ✓ to achieve further morbidity and mortality reduction in the remaining countries as a basis for the eventual elimination of measles in the Region;
- ✓ to establish surveillance indicators that can be used for the purposes of monitoring progress and certification of elimination; and
- ✓ to develop National Plans of Action for Measles as components of Multi-Year Immunization Plans and Annual Immunization Workplans (Annex 2).

4. STRATEGIES AND ACTIVITIES

4.1. Strategies

Three strategies need to be implemented for measles elimination: immunization, surveillance and laboratory support:

1. to achieve and maintain 95% population immunity to measles in each birth cohort within each district of each country in the Region (Immunization Strategy);
2. to develop and maintain effective surveillance in each country in the Region (Surveillance Strategy); and
3. to develop and maintain effective access to an accredited laboratory for each country in the Region (Laboratory Support Strategy).

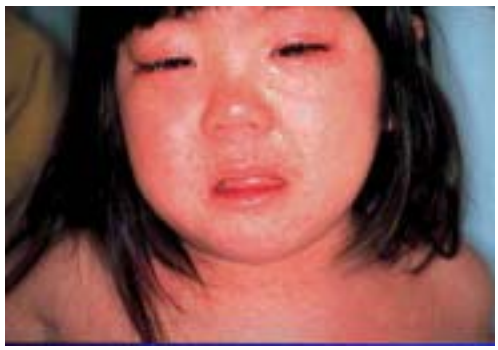
In addition, improved case management with associated vitamin A supplementation is a key component of measles morbidity and mortality reduction.

4.1.1 Immunization Activities

1. Establish and/or strengthen functional national coordination bodies.
2. Achieve effective and timely routine delivery of measles vaccine to each new birth cohort.

Measles Immunization

3. Achieve effective second opportunity measles vaccine delivery.
4. Routinely monitor population immunity.



Acute Measles

4.1.2 Surveillance Activity

1. Develop case-based surveillance (including response to cases) with laboratory confirmation.

4.1.3 Laboratory Support Activity

1. Provide laboratory support for measles diagnosis and virus tracking through a Regional network of accredited laboratories.

5. ANNUAL PROGRESS REVIEW

An annual Regional review will establish when it is appropriate to set an elimination target date. The criteria (see Annex 3) have been derived from the three strategies (immunization, surveillance, and laboratory support). They are:

- ✓ two opportunities for every child to receive measles vaccine;
- ✓ functioning case-based surveillance; and
- ✓ national access to an accredited measles laboratory.

See Annex 3 for current status.

6. IMPLEMENTING THE PLAN

Implementing the strategies requires an analysis of current and previous measles

Laboratory

control efforts in each country to develop a national plan, if one is not already in place (see Annex 2).

A three- to five-year measles plan as a component of national multi-year immunization plans and annual immunization workplans should be developed to address the three strategies: immunization, surveillance, and laboratory support and a national measles elimination target date.

6.1 Immunization

6.1.1 National Coordination

A national coordinating body, such as the inter-agency coordinating committee (ICC), or a measles-specific one, should be established or strengthened to:

- ✓ advocate for political participation in measles initiatives;
- ✓ coordinate multi-sectoral support;
- ✓ provide overall guidance in the development of national strategies and plans; and
- ✓ endorse National Measles Plans of Action.

To be effective, the coordinating bodies need competent, high level technical and political representation within their membership.

6.1.2 Measles First Dose Delivery

The delivery of the Expanded Programme on Immunizations (EPI) vaccines to new birth cohorts requires a substantial on-going detailed operational planning effort (microplans) at district and facility levels.

Each country should strengthen its microplanning capacity by focusing efforts and resources at district and facility levels and ensuring that these add to general EPI initiatives (including communication strategies to promote timely uptake of measles and other EPI vaccines).

6.1.3 Second opportunity for measles immunization

Countries need to offer children a second opportunity to receive measles vaccine to achieve 95% population immunity (Annex 4). The second opportunity needs to reach practically all children.

A national measles mass immunization targeting all age groups where population immunity is likely to be less than 95% is best where feasible. This mass immunization may be conducted as a one-round mass activity (over a 10 to 14 day period) or it may be staged according to specific country circumstances. The critical factor is achieving very high coverage, especially for the previously unreached.

A comprehensive set of options for delivery of the second opportunity need to be considered, comparing the advantages and limitations of each option to make the most appropriate decision for each country. Having chosen the method for the second opportunity, careful and consistent implementation will be needed to maintain population immunity at 95% or higher for each birth cohort.

For countries where it is not feasible to adopt a nationwide mass measles immunization strategy, the second opportunity should be started as soon as possible, if not already in place.

Monitoring of second opportunity coverage activities is needed, together with improved disease surveillance to guide decisions on mopping up immunizations.

Strategies that can be included in a comprehensive set of options comprise:

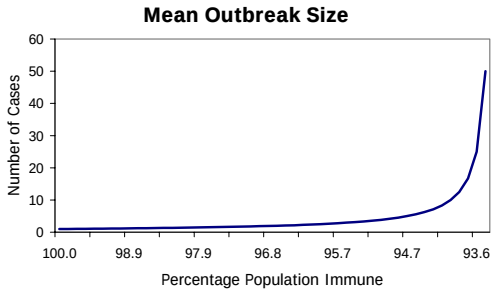
- ✓ routine two-dose measles immunization (with the second dose either as part of the schedule or regular national measles mass immunizations every four years, targeting children aged nine-59 months
- ✓ specific geographic location mass immunization where there is focal transmission of measles;
- ✓ periodic national measles mass immunizations as indicated by falling population immunity (five or more years after the initial wide age range mass immunization), targeting children from nine months to the birth cohort born the year before the initial wide age range mass immunization; and
- ✓ house-to-house or mopping up immunizations to identify and immunize children who have missed first and/or second dose opportunities.

Social mobilization specifically directed toward second opportunity activities is needed to achieve high coverage.

6.1.4 Monitoring population immunity

Population immunity can be monitored using routine and/or survey coverage data, and validated through disease surveillance. As re-introductions of measles virus are practically inevitable, the number of cases and size of outbreaks can provide an indication of population immunity, after adjusting for the number of cases that the surveillance system identifies. Mathematical models, using coverage and disease data, can be used to estimate immunity based on the size of an outbreak (see Figure 2). Also, serologic survey data can be used to estimate population immunity. But, these additional sources of information are not required as a routine.

Figure 2. Population Immunity as a function of outbreak size.



District and facility level analysis of immunity data needs to be undertaken regularly to guide management decisions for immunization delivery.

Details of immunization strategies and procedures are presented in the *Field Guidelines for Accelerated Measles Control in the Western Pacific Region 2002*.

6.2 Disease Surveillance

6.2.1 Overall Policy, Including Integration with acute flaccid paralysis (AFP) Surveillance

The national plan needs to address the development and dissemination of a policy on measles surveillance, including integration with AFP surveillance, investigation and responses to outbreaks and case management.

A process to integrate measles with AFP surveillance should be developed in countries that have not yet already done so, and where that will be the best process to

strengthen surveillance. The process should include, where needed, plans for a phased development of measles surveillance activities, from aggregated data reporting and analysis to case-based surveillance with laboratory confirmation. The process should also include the development of country-specific surveillance guidelines, standardized case investigation forms and procedures and plans for training and/or re-training staff. In addition, all countries should consider the health promotion and social mobilization implications of enhancing measles surveillance capacity and efficacy (see Annex 5).

6.2.2 Case Definitions, Reporting Forms and Process

Each country needs to prepare and disseminate measles case definitions, reporting forms, and the actions to take in response to suspected measles (rash and fever illness). The flow of completed forms and data from lower levels up and the flow of data and analyses from upper levels down must be specified, regular and routine.
Standard indicators for measles surveillance should be adopted to monitor activities. Examples of indicators for measles surveillance include:

- ✓ number of cases reported;
- ✓ age-specific measles incidence;
- ✓ number of annual measles deaths;
- ✓ number of hospitalized cases;
- ✓ immunization status of cases;
- ✓ percent of cases with blood taken for confirmation of diagnosis;
- ✓ number of outbreaks;
- ✓ percent of outbreaks investigated; and
- ✓ completeness and timeliness of facility and district reporting.

6.2.3 Investigation and Response

The policy also needs to define the investigation for individual cases and outbreaks and the response to them. As measles will not spread if population immunity is sufficiently high, there is not necessarily a need for an immunization response to an importation, unless the investigation shows that the area has low levels of immunization coverage.

6.2.4 Case Management

Optimal case management of measles cases will result in fewer deaths and severe complications. At minimum, health services can deliver vitamin A supplementation to ill children and children at high risk of vitamin A deficiency. Other interventions such as hospitalization will depend on the local resources.

Details of disease surveillance and outbreak investigation, reporting and response strategies are presented in the *Field Guidelines for Accelerated Measles Control in the Western Pacific Region 2002***.**

6.3 Laboratory Support

Measles cannot be reliably diagnosed clinically, especially when it becomes uncommon. All countries need access to an accredited national reference laboratory. A measles laboratory network of national diagnostic laboratories, Regional reference laboratories and global special laboratories is a key element of the plan.

Further details, including recommendations for blood specimen collection, are contained in the *WHO Manual for Laboratory Diagnosis of Measles 1999*.

6.4 Cross-cutting Issues

Measles elimination strategies will intersect with other immunization-related initiatives, including those with activities in:

- ✓ safe injection practices including the introduction of auto-disable syringes;
- ✓ safe disposal of used injection materials;
- ✓ introduction of rubella vaccine as measles rubella (MR) or measles-mumps-rubella(MMR), a simple, cost-effective addition to measles elimination activities;
- ✓ strengthening the investigation of and response to adverse events following immunization (AEFI); and
- ✓ health sector reform issues.

When implementing specific measles elimination-related activities, all countries should seek to build on the existing scheduled immunization program capacity in particular and health service delivery mechanisms in general.

7. FINANCING THE PLAN

Eliminating measles from the Region will have significant health and economic benefits for all countries. However, to do the task properly, financial resources over and above existing national budget and external support funds will be needed. Each country will need to prepare annual budget estimates (for three to five years), which include additional costings under the following headings:

- ✓ vaccines, syringes, needles and safety boxes;
- ✓ operational costs;
- ✓ waste disposal;
- ✓ surveillance costs;
- ✓ National Measles Laboratory establishment and maintenance costs;
- ✓ AEFI investigations;
- ✓ training/re-training costs;
- ✓ health promotion costs; and
- ✓ social mobilization costs.

At the Regional office level, budgets have been prepared reflecting the costs of coordination and oversight of activities already scheduled as well as the establishment and maintenance costs of the laboratory network (Annex 6).

ANNEX 1

PROGRESS IN MEASLES CONTROL IN THE WESTERN PACIFIC REGION

The Western Pacific Region is made up of 37 countries and areas that have a wide range of socio-economic, geopolitical, and demographic conditions. These varying conditions mean that what is appropriate in one country may not work in another. Therefore, there is a need for local flexibility, innovation, and initiative. However, a Regional plan with objectives and strategies can provide a basic framework for all countries.

In 1996, the Western Pacific Regional Plan of Action for Accelerated Measles Control was prepared. The stated objectives were:

(1) to reduce the burden of measles in every country of the Region, starting in 1999; and

(2) to develop measles surveillance to the extent that outbreaks of measles can be rapidly investigated and controlled, and epidemics predicted and prevented.

The stated strategies to achieve these objectives were:

(1) to evaluate the burden of measles disease through measles surveillance; and

(2) to reduce measles morbidity and mortality and prevent measles outbreaks.

Details of these strategies were: an active surveillance system integrated into the acute flaccid paralysis (AFP) surveillance system; laboratory confirmation of suspected measles cases; delivery of two doses of measles vaccine through extremely high routine first dose coverage and a second dose by mass immunizations or routine activities, as indicated.

The countries of the Region implemented this plan enthusiastically, but of course there is wide variation in measles control between countries. Overall, great progress has been made. (See Tables 1 and 2 below). In addition, the Annual Review Matrix (Annex 2 of this Plan) indicates progress by country and measles control activity.

Table 1. Measles Immunization Schedules, Reported MCV1 Coverage and Cases, 1999 – 2001, Selected Countries, Western Pacific Region

Country	Measles Immunization Schedule				Total Population (Thousands)	<1 Yr. Population (Thousands)	MV1 Coverage (%)			Reported Number of Cases		
	No. of Doses	Vaccine Used	Age, 1st Dose	Age, 2nd Dose			1999	2000	2001	1999	2000	2001
Australia	2	MMR	12m	4-5y	119,138	247	89	92	93	235	108	141
Brunei Darussalam	2	MMR	12m	10-13y	328	7.5	94	99	100	23	42	11
Cambodia	1	M	9m		13,104	448	63	65	59	13,827	12,237	3,761
China	2	M	8m	7y	1,275,133	18,835	98	97	79	61,840	71,093	88,962
Hong Kong, SAR, China	2	MMR	12m	6y	7,200	53	87	96	84	32	60	179
Japan	1	M	12m		127,096	1,214	96	96	98	-	22,497	22,552
Korea, Republic of	2	MMR	12m	4-6y	46,740	609	94	95	97	8	32,088	23,044
Lao PDR	1	M	9m		5,279	182	71	42	50	2,302	332	94
Macao, SAR, China	3	M & MMR	9m	15m; 5-6y	330	4.5	92	95	90	1	5	3
Malaysia	1	M	9-12m		22,218	521	88	88	88	2,576	6,187	2,198
Mongolia	2	M	8-12m	3y	2,533	55	93	94	95	10	925	10,677
New Zealand	2	MMR	15m	4y	3,778	54	82	85	85	106	65	65
Papua New Guinea	2	M	6m	9m	4,809	149	57	68	49	6,304	7,135	4,023
Philippines	1	M	9m		75,653	1,998	88	80	75	2,981	7,120	7,360
Singapore	2	MMR	15m	12y	4,018	50	86	93	89	65	141	408
Vietnam	1	M	9-11m		78,137	1,522	94	97	97	14,134	16,512	12,058
Total					**1,685,494**	**27,373**				**104,444**	**176,547**	**175,536**
Pacific Island Countries	**Doses**	**Vaccine**	**1st Dose**	**2nd Dose**	**Total Pop. (Actual)**	**<1 Population (Actual)**	**1999**	**2000**	**2001**	**1999**	**2000**	**2001**
American Samoa	2	MMR	12m	4y	59,585	1,812	99	90	92	0	1	0
Cook Islands	2	M	9m	5-6y	19,572	405	63	76	84	0	2	0
Fed. St. of Micronesia	2	MMR	12m	13m	120,370	2,654	79	85	84	0	0	0
Fiji	1	M	9m		825,995	17,893	95	-	90	20	-	17
French Polynesia	2	MMR	12m	8y	240,034	4,803	98	-	98	13	0	3
Guam	2	MMR	12m	4-6y	158,311	4,231	93	90	86	1	0	0
Kiribati	1	M	9m		89,077	2,423	62	80	-	2	0	0
Marshall Islands	2	MMR	12m	18m-6y	52,706	1,598	93	80	89	0	0	0
Nauru	1	MMR	12-15m		11,851	145	-	8	95	1	0	0
New Caledonia	2	MMR	12m	6y	216,046	4,476	-	-	-	1	-	0
Niue	2	MMR	15m	11y	1,918	27	100	100	100	0	0	0
Northern Mariana Is.	2	MMR	12m	4y	71,214	1,445	93	70	86	0	0	0
Palau	2	MMR	12m	15m	19,905	277	96	83	83	0	0	0
Samoa	1	M	9m		175,194	3,930	91	93	92	-	-	-
Solomon Islands	1	M	9m		428,835	15,376	59	-	-	-	-	0
Tokelau	1	M	9m		1,477	46	100	100	100	0	0	0
Tonga	2	M	9m	2-15y	99,521	2,399	97	-	93	6	0	4
Tuvalu	1	M	9m		10,069	224	94	-	100	0	-	0
Vanuatu	1	M	9m		195,633	5,754	94	94	94	12	52	7
Wallis and Futuna	1	MMR	12m		14,634	439	100	100	-	0	0	-
Total					**2,811,947**	**70,357**				**56***	**55***	**31***

Sources: World Health Organization. WHO vaccine-preventable diseases: monitoring system: 2001 global summary. Geneva, 2001. (WHO/V&B/01.34).
Also, WHO/UNICEF Joint Reporting Forms, 1999, 2000, 2001.

* NOTE: suspect cases; only 3 confirmed cases, all are imported virus in French Polynesia in 1999

Table 2.
Measles Mass Immunizations Up To 2001

Country	Type	Date	Target Age	Target Pop.	Coverage
American Samoa	None				
Australia	National	Jul-98	5 - 12 years	1,780,000	75
Brunei Darussalam	None				
Cambodia	Pilot National, phase 1 National, phase 2	Jan-00 Jan-01 Jan-02	9m - 59m 9m - 59m 9m – 14 years	228,532 171,772 2,500,000	82 90 99
China	Sub-national				
Cook Islands	National	Mar-98	9m - 14 years	6,524	85
Fiji	National	Nov-97	9m - 14 years	251,109	81
French Polynesia	National	Mar-98	8 - 12 years	25,000	77
Guam	None				
Hong Kong, SAR, China	National	1997	1 - 19 years	~900,000	97
Japan	None				
Kiribati	National	Feb-98	9m - 14 years	27,297	86
Korea, Republic of	National	May-01	8 years - 16 years	5,848,257	96
Lao People's Democratic Republic	Pilot National	Mar-00 Mar-01	9m - 59m 9m - 59m	64,040 636,730	95 ~85
Macao, SAR, China	None				
Malaysia	None				
Northern Mariana Islands	None				
Marshall Islands	Mop-up	1998			
Federated States of Micronesia	None				
Mongolia	National National National	Oct-94 May-96 Oct-00	3 – 7 years 9m - 11 years 9m - 7 years	218,034 558,187 ~300,000	75 97 ~97
Nauru	National	Dec-97	9m - 14 years	2,540	100
New Caledonia	National	Nov-97	6 years - 10 years	20,026	90
New Zealand	National	Apr-97	2 -10 years	~400,000	~75
Niue	National	Oct-97	9m - 15 years	796	99
Palau, Republic of	Mop-up	1998			
Papua New Guinea	National	Sep-97	9m - 59m	679,311	84
Philippines	National	Sep-98	9m - 14 years	27,000,000	~85
Pitcairn Islands	None				
Samoa	National	Apr-98	9m - 15 years	74,470	97
Singapore	None				
Solomon Islands	National	Jul-98	9m - 14 years	153,757	81
Tokelau	National	Jun-98	9m - 16 years	568	100
Tonga	National	Mar-98	9m - 14 years	35,458	94
Tuvalu	National	Mar-98	1 year - 14 years	3,033	100
Vanuatu	National	Apr-98	9m - 14 years	77,850	95
Vietnam	Pilot Enlarged pilot Pilot National, phase 1	Nov-99 Dec-00 Oct-01 Mar-02	9m - 10 years 9m - 10 years 9m - 10 years 9m - 10 years	253,295 327,500 1,554,120 6,729,171	99 98 99 99
Wallis and Futuna	None				

ANNEX 2

DEVELOPMENT OF A NATIONAL PLAN OF ACTION

Each country/area of the Western Pacific Region should develop a National Plan of Action for/towards Measles Elimination which is a component of the Multi-Year Immunization Plan and Annual Workplans. For countries that are not yet ready to set a target date for elimination, the plan should include a process for working towards setting that date. The plan should include:

- background information about the level of achievement for measles control;
- establishment of a national measles control or elimination task force, through the ICC;
- an overview of measles surveillance in the country;
- an activity plan for measles surveillance, including:
    - active measles surveillance and integration with AFP and NT active surveillance;
    - the objectives of the Measles Surveillance System;
    - the target surveillance population;
    - standard case definition;
    - case investigation;
    - data management;
    - indicators and data flow; and
    - a plan for development and expansion of the system;
- information on the size of the target population for routine and supplementary measles immunization activities, number of districts with outbreaks reported and investigated, mapping of measles cases;
- an activity plan for supplementary immunization activities in the country;
- an activity plan for scheduled immunization activities;
- a budget for implementation of activities; and
- the time schedule for programme activities.

ANNEX 3

ANNUAL REVIEW MATRIX

Country/Area	Planning for Measles Elimination	Second opportunity activities	Case-based surveillance	Access to accredited laboratory	Second opportunity activities	Case-based surveillance	Access to accredited laboratory	Target	Status
	Planned				Implemented				
Australia	X	X	X	X	X	X	X	YES	E
Brunei Darussalam	X	X	X	X	X	X			R
Cambodia	X	X	X	X	X	X			R
China		X		X	X				N
Hong Kong, SAR	X	X	X	X	X	X			R
Japan			X	X					N
Lao PDR	X	X	X	X	X				R
Macau, SAR	X	X	X	X	X	X			R
Malaysia	X	X	X	X	X				R
Mongolia	X	X	X	X	X	X			R
New Zealand	X	X	X	X	X	X		YES	E
Pacific Island Countries	X	X	X	X	X	X	X		E
Papua New Guinea				X					N
Philipppines	X	X	X	X	X	X		2008	E
Republic of Korea	X	X	X	X	X	X		2005	E
Singapore	X	X	X	X	X	X			R
Viet Nam	X	X	X	X	X			YES	E

N	= Not ready for elimination
R	= Ready for elimination (all elements planned)
E	= Elimination mode

ANNEX 4

MEASLES VACCINE SECOND OPPORTUNITY STRATEGIES

Second opportunity for measles immunization

To achieve the high level (95%)of population immunity required to eliminate measles, requires very high coverage with two doses of measles vaccine. Each country will need to determine the best way of achieving this. Even with a two-dose schedule, a second opportunity may be needed if coverage of the scheduled doses is not high enough.

In all countries that have only had a single scheduled dose of measles vaccine, a mass immunization activity is needed. Even with 100% coverage for a single dose of measles vaccine, population immunity is not more than about 90% immunity.

An epidemiological analysis of disease and coverage data can identify the cohorts who are likely to have less than 95% immunity. There is an immediate need to immunize these cohorts while still of school age, as mass immunizations in older groups are more challenging.

Mass immunizations

A mass immunization can rapidly reduce measles morbidity and mortality. As a general rule, mass immunizations should deliver measles-containing vaccine only, and should not attempt to deliver other injectable vaccines. However, vitamin A supplementation should be part of supplementary measles immunization activities in populations at risk for vitamin A deficiency, because vitamin A deficiency increases the risk of serious sequelae and death from measles infection. The following strategies should be considered:

(1) One-round national measles mass immunization

The objective of the initial mass vaccination is to substantially reduce measles cases and deaths. This intervention can achieve such reductions years earlier than the introduction of a two-dose measles schedule, resulting in fewer cases and deaths. The target age of the activity should include those age groups where more than 5%-10% of the population is susceptible. Experience in other regions indicates that, in countries with good measles control, this is usually from 9 months to 14 years of age, while, in countries with poorer measles control, the upper age limit will be less (10 years of age or younger). An increased number of deaths from measles among young infants can justify reducing the lower limit to six months. The target population should be vaccinated regardless of previous immunization status or history of disease. The objective is to reach >95% coverage on a district basis (third administrative level) countrywide. Very high coverage should be reached in areas not reached by scheduled immunization services. Careful attention must also be given to areas that, although within the reach of scheduled immunization services, are usually only covered poorly because of local constraints. Slum areas or squatter settlements, dispersed riverside populations, very remote villages or nomadic people, and "institutionally neglected" populations are examples of this category.

Due to the increased resource requirements for the successful implementation of a large-scale mass immunization activity with measles vaccine, it is recommended that countries pilot the intervention on a small scale, targeting epidemiologically meaningful areas. Major factors that will contribute to successful implementation include:

- a very high level of political commitment toward the initiative;
- effective coordination of activities at the national and lower levels;

- effective planning, with careful distribution of fixed sites and mobile teams according to population distribution and careful attention to populations with a high risk of remaining as foci of measles transmission after the event;
- a single vaccine intervention;
- timely provision of sufficient vaccine, logistics and funds for operations;
- effective social mobilization, with appropriate strategies according to the local cultural settings;
- use of tally sheets to record vaccinated children (nominal lists of target populations should be used in exceptional circumstances only as they usually reduce the speed and quality of services in fixed sites, increase the error in coverage estimates – usually overestimation – and do not help mobile teams working in critical settings like markets, etc.);
- fully dedicated personnel during the activity; and
- effective supervision of vaccination teams.

More detailed information regarding the planning and implementation of measles mass immunization activities, including immunization safety requirements, to be provided in the *Field Guidelines for Accelerated Measles Control in the Western Pacific Region 2002*.

(2) One-round subnational measles mass immunization

For countries with focal measles transmission, the implementation of a one-round subnational measles mass immunization campaign can be appropriate. The technical requirements and factors that will contribute to its success are the same as for national measles mass immunization activities (see above). A national mass measles immunization may also be delivered progressively through several subnational mass immunizations.

(3) Follow-up measles mass immunization

Countries that have already conducted an initial national measles mass immunization may need supplementary mass immunization to decrease the newly accumulated susceptibles, and should plan to conduct a subsequent national measles mass immunization every four years. The target age group should be 9-59 months, unless the local epidemiology of measles indicates a wider age group should be targeted.

In countries where the current control strategies have already resulted in the interruption of indigenous transmission of measles, it is imperative to continue to achieve excellent coverage with two doses of measles vaccine and excellent surveillance. There may still be a role for supplementary measles activities in such countries. Data on the current epidemiology of measles in the country is essential to decide when, where and whom to target in any supplementary immunization activity. Periodic mass immunizations may be required to decrease the number of newly accumulated susceptible children so as to maintain population immunity above 95%.

ANNEX 5

ESTABLISHING A CASE-BASED MEASLES SURVEILLANCE SYSTEM

The establishment of an effective measles surveillance system is a key factor for the successful implementation of the measles accelerated control or elimination initiative in every country.

The main objectives of the measles surveillance system are:

(1) to identify all areas of measles transmission in the country;

(2) to measure the impact of measles control and elimination strategies; and

(3) to detect the occurrence of measles outbreaks in order to ensure timely and appropriate outbreak response.

For countries with an elimination goal, it is imperative that all cases are reported.

Strategic approach to building surveillance systems

It is recommended that countries follow a phased or step-by-step approach in building their case-based measles surveillance systems in order to ensure high quality for the whole process.

Initial stage

- ✓ First of all, measles should be a *reportable* disease for all areas of the country and for all ages.
- ✓ Case identification should be based on a *standard case definition* and case-based data should be collected in all countries (see below for sample data collection form). All routine reports should contain individual case data on date of rash onset, age, immunization status, location and outcome (if the patient died or not). The recording of surveillance case investigation data should be done on standardized case investigation forms.
- ✓ To improve case detection and case investigation, active surveillance for measles should be implemented in major hospitals, with zero reporting on a regular basis, to detect and investigate all cases managed in these hospitals. The activity should be integrated into the existing active surveillance systems for cases of acute flaccid paralysis (AFP) and neonatal tetanus (NT). Blood specimen collection and serological testing should be carried out according to the capacity of the existing national measles laboratories.

Outbreak investigation and response

Measles outbreak investigation is part of the recommended surveillance activities and should be conducted by provincial- and national-level personnel. The investigation should include limited serological testing of blood specimens. Health facilities not included in the active surveillance system should report measles outbreaks immediately.

In the case of a confirmed outbreak in a population, it is important to plan a systematic response, based on available data. The convening of a response team is essential to ensure quality decisions and coordination. It should be understood that the immunization response in most outbreaks usually occurs too late to blunt the impact of the outbreak. However, in closed communities or institutions, such as refugee camps, hospitals or military barracks, it may be necessary to conduct supplementary immunization activities as soon as possible. In refugee camps, vaccination of all children below five years of age is indicated as soon as they arrive in the camp. Delay in implementing this

recommendation may result in high morbidity and mortality. It is also important to note that the priority during outbreaks is to provide appropriate treatment and reduce mortality.

(More information on measles outbreak investigation and response is provided in the *Field guidelines for measles accelerated control in the Western Pacific Region 2002*.)

Expansion stage

As the measles accelerated control initiative matures, active surveillance for measles should be expanded to cover all ages and all districts. Case investigation should be conducted at the district (third administrative level) and should include laboratory confirmation of cases (>80% of cases should have one blood specimen collected from 4-28 days after onset of rash). All outbreaks should be detected, reported, investigated and confirmed by the laboratory. All surveillance and laboratory data should be entered into an electronic database at the national level to make data management efficient (facilitating consolidation, analysis and reporting, including data feed forwarding to other government departments, other agencies and the WHO Regional Office).

Consolidation stage

Active surveillance for measles should be comprehensive, complete, timely, sensitive and reliable. It is anticipated that immunization activities will result in markedly reduced measles transmission, so all health care facilities should report immediately all suspected measles cases and make supplementary zero reports when there are no cases. All suspected cases must be investigated rapidly and confirmed or discarded by laboratory testing. All reports should contain individual case data obtained from fully investigated cases.

Detailed information on measles surveillance and data management requirements, including reporting and analysis to be provided in *Field guidelines for measles accelerated control in the Western Pacific Region 2002***.**

ANNEX 6

Estimated Additional External Funds Needed for Currently Planned Activities (in US$)

Year	Periodic Immunization			Country Level	Regional Level		Total
	Bundled Vaccine	Operational Costs	Waste Disposal	Surveillance and Immunization Safety	Coordination	Laboratory Network	
2003	$9,207,000	$2,300,000	$907,000	$280,000	470,000	$375,000	$13,539,000
2004	$47,000	$40,000	$8,000	$280,000	470,000	$377,000	$1,222,000
2005	$304,000	$340,000	$58,000	$320,000	470,000	$377,000	$1,869,000
Total	$9,558,000	$2,680,000	$973,000	$880,000	$1,410,000	$1,129,000	$16,630,000

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR THE WESTERN PACIFIC

WESTERN PACIFIC REGIONAL PLAN TO IMPROVE HEPATITIS B CONTROL THROUGH IMMUNIZATION

Manila, Philippines
January 2003

(WP)ICP/EPI/5.2/001-E English only

WESTERN PACIFIC REGIONAL PLAN TO IMPROVE HEPATITIS B CONTROL THROUGH IMMUNIZATION

Not for sale

Printed and distributed by

World Health Organization
Regional Office for the Western Pacific
Manila, Philippines

January 2003

CONTENTS

SUMMARY

Hepatitis B virus (HBV) infection is an important public health problem, especially in the Western Pacific Region. A safe and effective vaccine has been available for 20 years. It is now used in every National Immunization Programme (NIP) in the Region. Hepatitis B vaccine (HepB) is the first vaccine available that prevents cancer.

Current global estimates of measles and HBV-related deaths suggest that the two viruses currently cause about the same number of deaths per year globally, but in the Region there are over 10 times as many annual deaths from HBV as from measles. Of the 278 000 estimated deaths caused by HBV infection in the Region, nearly all are from the consequences of chronic infection, mostly decades after the initial infection at birth or early childhood. Therefore, the regional objective is to prevent chronic HBV infection. The milestone to measure country progress is to achieve (five years after starting the hepatitis B immunization programme):

HBsAg prevalence <1% in five-year-olds born after routine immunization started.

An intermediate milestone of <2% may be appropriate among hard-to-reach populations. Countries that have already achieved the milestone of <1% prevalence need to set a more challenging target.

For countries to achieve the objective, the following actions are suggested:

- establish/strengthen a national hepatitis B control plan (as part of an overall EPI plan) by 2003;
- establish a *system* to monitor delivery, and a *target date* for achieving at least 80% coverage, of a timely scheduled birth dose (within 24 hours of birth) by 2004;
- include receipt of three doses of HepB for a child to be 'fully immunized by the EPI' by 2003 – except where only babies of HBsAg positive mothers are offered immunization; and
- achieve full EPI immunization of at least 80% (ideally 95%) of each birth cohort and in every district by 2005.

A safe and effective vaccine is available and in use throughout the Region. Improving its use, the key for hepatitis B control, requires improving routine immunization services, and the above actions provide the framework for that improvement.

Achieving and maintaining high immunization coverage in infants is the most important strategy for the control of hepatitis B. A timely birth dose (within 24 hours of birth) is also needed to prevent perinatal transmission (a major source of chronic HBV infection in the Region).

Monitoring of hepatitis B immunization programmes is carried out primarily through coverage assessment, including monitoring delivery of a timely birth dose. The impact on disease cannot be monitored as with other vaccine-preventable diseases, because of the long time lag before complications develop from chronic infection and because those complications are not exclusively caused by HBV. Therefore, impact is assessed through serosurveys of HBsAg. Countries should undertake at least one serosurvey in vaccinated cohorts to validate the impact expected from reported immunization coverage.

The nature of hepatitis B means that special advocacy and social mobilization efforts are needed. The efforts need to include ensuring that health workers are fully informed as to the importance of hepatitis B immunization, as the disease burden is sometimes not recognized and vaccinating newborn infants may be difficult in some societies.

GLOSSARY

BCM	Baby of carrier (HBsAg positive) mother
Carrier	Person with long-term (chronic) HBV infection.
DTP	Diphtheria-tetanus-pertussis vaccine – a combination product of the three vaccines that protects against the three diseases
DTP3	The third dose of diphtheria-tetanus-pertussis vaccine
DTP-HepB	A combination of two vaccines that protects against the four diseases
DTP-HepB3	The third dose of DTP-HepB – the final one in the series. For monitoring this should be considered as the HepB3 dose, even if a birth dose is given making it the fourth dose of hepatitis B vaccine.
EPI	Expanded Programme on Immunization
FIC	Fully immunized child – a child that has received all the recommended vaccines by a specified age (usually by 12 months)
HbcAg	Hepatitis B core antigen – a protein found in the core of the virus
HBeAg	Hepatitis B 'e' antigen –indicates greater infectivity in chronic infection
HBsAg	Hepatitis B surface antigen: a protein from the virus's coat. A positive test for HBsAg indicates active HBV infection. The immune response to HBsAg provides the basis for immunity against HBV, and HBsAg is the main component of HepB.
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma, or primary liver cancer - a major complication of chronic HBV infection; usually fatal
HepB	Hepatitis B vaccine (can be plasma-derived or recombinant)
HepB3	The third and final dose of HepB – three doses recommended for protection
NIP	National Immunization Programme
Plasma-derived HepB	HepB manufactured from the plasma of HbsAg+ carriers by extracting the HBsAg
Recombinant HepB	HepB manufactured from a genetically modified yeast or mammalian cell with the gene to produce HBsAg
Seroprevalence	Percentage of a population positive for a specific antibody (e.g. to HBsAg) or antigen (e.g. HBsAg)

Acknowledgements: This paper was prepared with guidance and support of David Hipgrave, Basil Rodriques, Craig Shapiro and John Waldon. The following provided helpful comments and suggestions on earlier drafts: Bheemayya Badesab, Maureen Birmingham, Jean-Paul Chainé, Nora Dellepiane, Unyeong Goh, Richard Guan, Andy Hall, Umit Kartoglu, Kalsom Latif, AK Metai, Julie Milstien, Sandor Milne, Chris Nelson, Chong Jin Oon, Hitoshi Oshitani, Datin Salleh and Fred Shaw. A working group meeting on hepatitis B also provided material for the plan.[1] The Technical Advisory Group on the Expanded Programme on Immunization and Poliomyelitis Eradication (TAG) reviewed the plan, and recommended actions to monitor country progress.

1 BACKGROUND

1.1 Purpose and focus of the plan

Hepatitis B vaccine (HepB) has been used in every National Immunization Programme (NIP) in the Western Pacific Region since December 2001. This plan builds on this achievement – its aim is to improve hepatitis B control through immunization by identifying the priority strategies and activities to reduce hepatitis B virus (HBV) infections. The primary aim of hepatitis B control is to prevent chronic infection because it leads to the major burden of HBV-related disease. Reducing chronic infection rates can eventually lead to the eradication of HBV.

Unlike other Expanded Programme on Immunization (EPI) diseases, hepatitis B infection rarely causes symptoms in children. It causes a chronic infection that can lead to cirrhosis or liver cancer (hepatocellular carcinoma), usually decades after infection. So, HBV is relatively invisible and often not identified as the cause in these preventable deaths. Therefore, specific strategies are required for advocacy as well for assessing the effect of immunization – both key factors to improve control.

Background information about HBV, consequences of HBV infection, and HBV epidemiology can be found in Annex 1 and information on HepB in Annex 2. More information is available from various sources including WHO guidelines,[2] and from the Internet, including: www.cdc.gov/ncidod/diseases/hepatitis/b/index.htm; www.immunize.org/hepb/index.htm; www.hepatitis-central.com/index.html; www.hepnet.com/hepb.html; www.hepb.org; and www.hepatitisb.org. A training resource for hepatitis B is available at: www.childrensvaccine.org/html/ip_clinical.htm#hbvtrain.

1.2 Control options

Hepatitis B is unique among bloodborne and sexually transmitted infections because a highly effective vaccine prevents transmission. Additional control options (e.g. screening of blood products, promotion of safe sex) are important, but this plan focuses on immunization as the most cost-effective method.

Another important control strategy is ensuring the safety of injections, including monitoring adverse events following immunization (AEFI).[3] These topics are not covered in this plan as they are covered in a separate Regional plan.[4]

1.3 HepB use in Western Pacific Region

HepB first became commercially available in 1982. In 1992, WHO recommended the integration of HepB into NIPs by 1995 for countries with HBsAg prevalence of 8% or more and for all countries by 1997.[5] By the end of 2001, only 136 (71%) of the 191 WHO Member States had done so. In contrast, HepB was part of the NIP in all countries in Western Pacific Region (Table 1, Annex 3), with support from the Global Alliance for Vaccines and Immunization (GAVI).

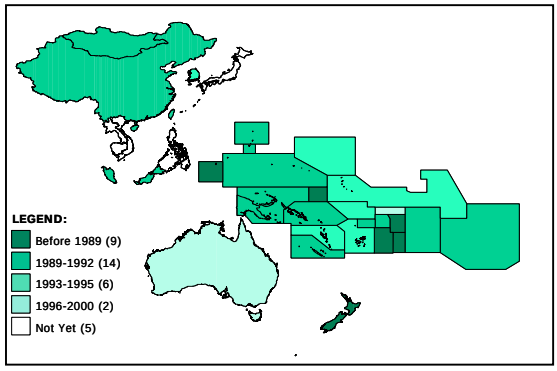
However, HepB is not fully integrated in some countries as shown by these indicators (see Table 2, Annex 3 for data):

- HepB routinely offered to all infants;
- HepB included in the definition of a fully immunized child (FIC);
- coverage of HepB3 is within five percentage points of DTP3; and
- funding for HepB immunization (as for other EPI vaccines).

All countries in the Region routinely offer HepB, with these exceptions:

- the Lao People's Democratic Republic and Cambodia are phasing in DTP-HepB (through GAVI support) – with the aim of achieving national coverage by 2004 and 2005, respectively;
- Viet Nam's local vaccine production capacity is sufficient only for about 15% of births; from 2003 (through GAVI support) vaccine will be provided for all infants.

Figure 1. Year HepB routinely offered to all infants



- China has user fees which limit access; these will be reduced from 2002 (through GAVI support) - see Annex 3; "Impact of user fees".
- The Philippines has not yet been able to afford to procure vaccine for the entire birth cohort (~80% in 2001).
- Japan has succeeded in reducing chronic HBV infection with a 'high-risk' approach: offering vaccine only to babies of HBsAg positive mothers and not to all infants.

All countries include HepB immunization in the definition of 'fully immunized' - with the exception of those countries that are not yet offering vaccine to all infants. Coverage for HepB3 is generally the same as for DTP3 in most countries, with the major issue at present being data quality. The funding for vaccines varies in the Region, but all countries offer HepB on the same basis as other EPI vaccines, except in China (see above and Annex 3).

1.4 Disease burden

1.4.1 Acute hepatitis B cases

Acute hepatitis B represents only a small part of the overall disease burden, and there are only limited data in the Region on the burden of acute hepatitis B. There is a variable level of reporting in different countries; many do not routinely test hepatitis cases to distinguish those caused by HBV as distinct from those caused by other viruses. If the only test used is for HBsAg, it will not differentiate acute from chronic infection.

Some countries have notification data on acute hepatitis B cases that show a decline following introduction of immunization (Table 3, Annex 3). Although these data suggest that HepB immunization has led to a decline in acute hepatitis B cases, there may also be other factors accounting for the declines.

1.4.2 Consequence of chronic HBV infection (carriage)

It is estimated that 15%-25% of people with chronic HBV infection die prematurely from Hepatocellular carcinoma (HCC) or cirrhosis caused by the infection.[6 7 8] However, data on deaths from these conditions are limited, and not all of deaths from HCC or cirrhosis are due to HBV.

Some countries have undertaken special studies to assess how many deaths of the total deaths caused by cirrhosis and HCC can be attributed to HBV. In New Zealand, an estimated 100 deaths per year are attributable to chronic HBV infection,[9] or about 0.3% of all deaths, even though overall rates of carriage are relatively low.

The full impact of immunization on the consequences of chronic infections will not be seen for decades, but there is already evidence of decreased HCC incidence in immunized children,[10] and even in adults.[11]

1.4.3 Modelling disease burden

Given the difficulties of measuring the disease burden, WHO has developed a model that estimates the current global burden at 360 million chronically HBV infected people, 5.7 million and HBV-related cases and 520 000 deaths per year.[12] Over half of the annual death toll (278 000) is in the Western Pacific Region, which has only about a quarter of the global population. It should be noted that these estimates are lower than previous estimates as they have taken into account competing mortality. In other words people with chronic HBV infection who die prematurely from other causes are not included in the estimate.

The model estimates that 69% of HBV-related deaths are from HCC (with or without cirrhosis), 21% from cirrhosis and 10% from acute hepatitis, globally. In contrast, 92% of the morbidity is from acute hepatitis, 6% from HCC and 2% from cirrhosis, globally.

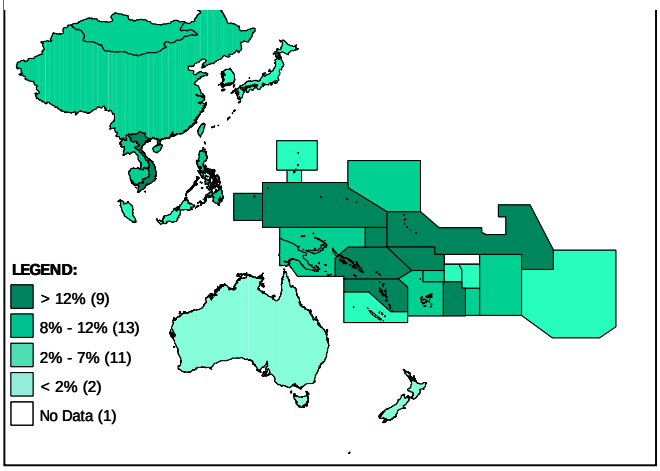
1.4.4 Comparison with measles disease burden

The relative importance of hepatitis B in the Region as well as the potential for control is illustrated by comparing the estimates of 1999 measles deaths. As a result of the Region's successful immunization programmes, it is estimated that measles deaths have been reduced by over 95%, and only about 2% of global measles deaths occur in the Region (about 20 000 of the global total of 875 000 measles deaths). In contrast the Region has over half of the estimated HBV-related deaths at 278 000 per year.

1.5 Seroprevalence and impact of immunization

Available data on HBsAg prevalence show a wide range of values among countries and within some of the countries. The results of a limited review undertaken for this Plan have been pooled to provide an estimate of prevalence. The estimates from some countries from studies are biased upwards as larger studies have been undertaken in higher-risk populations (e.g. in New Zealand). The pooled estimate was then used together with other estimates (including official country estimates) and a 1997 WHO estimate to provide a 'best estimate' of pre-vaccine HBsAg prevalence for each country (Table 3, Annex 3).

Figure 2. Chronic HBV infection (seroprevalence)



Where there had been an assessment of impact for vaccinated children, seroprevalence has been reduced by over 85%, with the exception of Mongolia, which had an estimated decline of only 50% (Table 3, Annex 3). It has been suggested that this may have been the result of vaccine being frozen during transport.[13]

2 REGIONAL OBJECTIVE AND COUNTRY MILESTONES

The Regional objective is to reduce chronic HBV infection. The milestone to measure country progress is to achieve (five years after starting the hepatitis B programme):

HBsAg prevalence <1% in five-year-olds born after routine vaccination started

An intermediate milestone of <2% may be appropriate among hard-to-reach populations. Countries that have already achieved the milestone of <1% prevalence need to set a more challenging target.

Humans are the only known hosts of HBV, thus making eradication possible (i.e. eradicating the virus without the need for further control measures). However, HBsAg positive persons can remain infectious for life, so eradication will require several generations. The first step towards eradication is to reduce infections in young children, as most chronic infections are acquired by the age of five years. For countries to achieve the objective, the following actions are suggested:

- establish/strengthen a national hepatitis B control plan (as part of an overall EPI plan) by 2003;
- establish a *system* to monitor delivery, and a *target date* for achieving at least 80% coverage, of a timely scheduled birth dose (within 24 hours of birth) by 2004;

- include receipt of three doses of hepatitis B for a child to be ‘fully immunized by the EPI' by 2003 – except where only babies of HBsAg positive mothers are offered immunization; and
- achieve full EPI immunization of at least 80% (ideally 95%) of each birth cohort and in every district by 2005.

3 NATIONAL HEPATITIS B CONTROL PLAN

Each country should establish or strengthen its national plan of action for hepatitis B control. An expert group of stakeholders in hepatitis B control should be convened to help develop and implement the plan. The hepatitis B plan needs to be part of the overall EPI plan, while ensuring that the specific issues outlined in this document are adequately addressed. In particular, advocacy and social mobilization, monitoring and evaluation require specific efforts for hepatitis B.

Monitoring and improving the knowledge of health workers is an important part of improving the coverage and quality of immunization services. An instrument to assess health worker knowledge on EPI is included as Annex 4, for local adaptation and development.

The national plan should include the public health response when a case of hepatitis B infection (chronic or acute) is identified. It should define which groups, other than infants, should be offered immunization. Any extension of immunization should be based on careful epidemiological and economic analysis, and may include:

- those who missed out on immunization as infants (‘patch-up’);
- cohorts born before HepB was offered (‘catch-up’);
- contacts of HBsAg positive persons; and
- high-risk groups (e.g. sex workers, health workers).

For all countries, the priority is protecting infants through the routine EPI. Providing catch-up and patch-up of children under the age of five years is likely to be the most cost-effective strategy, as these are the children most likely to acquire chronic infection. It is up to each country to prioritize other groups for publicly-funded immunization.

4 ROUTINE IMMUNIZATION STRATEGIES

Strengthening routine immunization services in order to immunize at least 80%, and ideally 95%, of each birth cohort, is the most important strategy for hepatitis B control. In addition, the following specific activities are recommended:

- reducing visits by scheduling HepB at the same time as other vaccines;
- including HepB immunization in the definition of 'fully immunized child';
- comparing HepB3 and DTP3 coverage, and addressing any differences (as part of overall assessment of access and drop-out);
- monitoring timeliness of delivery of birth dose; and
- ensuring that HepB is not frozen (see Annex 2).

4.1 Rationalizing immunization schedules

HepB can be scheduled at the same time as other EPI vaccines:

Table 1. Scheduling of HepB and DTP.

Age*	Monovalent vaccine			Combination vaccine
	DTP	HepB (no birth dose)	HepB (birth dose)	
Birth			HepB-birth	HepB-birth
6 weeks	DTP1	HepB1	HepB2	DTP-HepB1
10 weeks	DTP2	HepB2		DTP-HepB2
14 weeks	DTP3	HepB3	HepB3	DTP-HepB3

*Age given is flexible, with the recommended ages being the earliest possible ones. DTP is given at later ages in many countries, and need not be changed; but HepB should be given at same visit as DTP.

Many countries are still giving HepB at other times (Table 1, Annex 3). Reducing the number of visits increases the likelihood of children being fully immunized.

4.2 Birth dose

Protecting children against perinatal infection is a high priority because up to 40% of chronic infections are acquired perinatally in the Region. Timely delivery of a birth dose (and a second dose within two months) for all children is the preferred strategy. The alternative of antenatal testing to identify HBsAg positive mothers and immunize the babies of HBsAg positive (carrier) mothers (BCMs) is impractical for most countries in the Region.

A birth dose is part of the immunization schedule in all but seven countries and areas of the Region: four with antenatal screening and three with limited access to infants at birth. In the first group, BCMs are offered vaccine and/or hepatitis B immunoglobulin (HBIG) (Japan, New Caledonia, New Zealand, Wallis and Futuna). In the second group, many or most births are not attended (Table 1, Annex 3: Cambodia (62%), Lao People's Democratic Republic (79%) and Philippines (44%)). In countries with limited access to infants at birth and with low coverage, the priority is to deliver three doses of HepB to as much of the infant population as possible. However, even in these countries, a birth dose will be feasible for many babies.

Given its importance, countries should establish a target date to achieve at least 80% coverage for receipt of a timely birth dose. Routine reporting systems, suitably modified, can be used to monitor the percentage of births given a timely birth dose.

WHO recommends that the birth dose should ideally be given within 24 hours of birth, as it is likely that the earlier the vaccine is given, the more likely that infection will be prevented. However, the birth dose may be of value in preventing perinatal infection even if given later (see Annex 2), and it should be given on first contact, if not at birth.

WHO needs to assist countries to explore strategies to increase the timely delivery of a birth dose for babies born outside health facilities, as part of comprehensive maternal and child health care.

4.3 Uniject™ and use of the vaccine outside the cold chain

The availability of monovalent hepatitis B vaccine in prefilled single-dose injection devices (e.g. Uniject™) can facilitate the administration of the vaccine by birth attendants to infants delivered at home.[14]

In order to reach children in remote areas where there is no cold chain, the addition of vaccine vial monitors (VVMs) provides a new opportunity to use these vaccines after exposure to ambient temperature for several days or even weeks. VVMs are now available for most UNICEF-procured vaccines, including HepB. VVMs of varying stability are available, and provide assurance that cumulative heat exposure has not exceeded the limit for that vaccine. As HepB vaccine is relatively heat-stable and retains its potency even after

storage out of the cold chain, this may be especially useful for the timely provision of a birth dose provided the vaccine is not frozen; HepB is inactivated by freezing. However, caution will be needed to ensure that messages about the importance of the cold chain for other vaccines are not compromised by use of HepB after storage at ambient temperature.

4.4 User-fees

Ideally there should be no out-of-pocket expenses for immunization because other people will also benefit from another person's immunization, and immunization is a public good.[15] User fees discourage uptake and increase inequities in health. However, where user fees exist, any charge for HepB should be the same as for other EPI vaccines.

5 MONITORING AND EVALUATION

Reasons for monitoring or evaluation include:

- identifying problems in programme design, implementation, and/or delivery;
- sustaining the programme by demonstrating impact;
- carrying out advocacy and social mobilization; and
- monitoring progress towards achieving goals.

Unlike other vaccine-preventable diseases, the impact of immunization is not immediately visible, and requires special methods for monitoring.[16] There are four outcomes that will show the impact of hepatitis B immunization:

- coverage;
- seroprevalence;
- acute disease surveillance; and
- chronic liver disease surveillance.

5.1 Coverage

The primary method for countries to evaluate their programme is through monitoring immunization coverage. Countries must monitor their programme and produce reliable data on the number and percentage of infants that complete the course of hepatitis B immunization by the age of one year. Coverage monitoring should also include the timeliness of the birth dose, access, dropout, and comparison with other vaccines. It should be done regularly (at least quarterly) and down to district level.

Coverage surveys can be done periodically (e.g. every three years) to validate routinely reported data as well as to find out reasons for failure to immunize.

5.1.1 Wastage

Routine coverage data, together with vaccine stock data, can be used to generate wastage data. As HepB, and even more so DTP-HepB, is relatively expensive, efforts to reduce vaccine wastage are important. The key step is having some process for monitoring wastage and identifying the different types of wastage.

It must be borne in mind that attempts to reduce vaccine wastage must not be at the cost of immunization coverage. Effort should be exerted to reach and immunize each child. Failure to do so may prove costly in the end.

5.2 Seroprevalence

Every country should undertake at least one survey of HBsAg prevalence in vaccinated cohorts within five years of vaccine introduction to validate the expected impact on carriage from immunization coverage data. Children at age one year should be sampled to measure impact and at age five years to assess horizontal transmission. As most chronic HBV

infections are acquired by age five years, the seroprevalence targets can be assessed in children aged about five years who were born after routine immunization started.

The sample size should be adequate to show with 95% confidence HBsAg prevalence of <1%. Ideally, such a survey should be population-based to facilitate interpretation and increase its value. Guidelines for undertaking a random sample are being prepared by WHO, including advice on sample sizes and the selection process.[17] In areas without the laboratory capacity, the testing may be done with a strip test (see "Rapid field tests for HbsAG", below). The population of primary interest is young children, as impact on them can be most immediately monitored.

Convenience samples can be undertaken using blood taken for other purposes (e.g. taken for clinical tests in a hospital). Tests taken from blood donors or antenatal women are other options. While using these samples is more convenient and easier, the selection biases mean that the results may not be representative of the general population. In some countries "informed consent" and related ethical issues may arise, even if the blood is tested anonymously.

5.3 Acute disease surveillance

Acute hepatitis B surveillance, especially in sentinel sites, may be considered as an additional means to monitor impact if a system can be established within available resources. Surveillance data can also be used to identify certain risk groups who should be offered immunization. However, it is not essential to implement such monitoring for the immunization programme.

5.4 Mortality from liver disease

While this is an option for countries with cancer registries and reliable routine mortality statistics, it is not a realistic option for most.

5.5 Laboratory tests for diagnosis of hepatitis B

The diagnosis of HBV infection or assessment of immunity to HBV requires laboratory detection of HBsAg and anti-HBs; testing for anti-HBc may also be necessary. An established laboratory with adequate equipment and quality control is needed. ELISA tests are most sensitive and specific. Tests for HBsAg and other markers are commercially available, and may be interpreted as indicated:

Antigen/antibody	**Interpretation**	**Indication**
HBsAg	Potentially infectious person – present weeks before to several months after symptoms onset and persists in chronic infection	Infection
HBeAg	Replication of virus and high infectivity	Infectivity
Anti-HBs	Immune to HBV (vaccine or past infection)	Immunity
Total anti-HBc	Acute, chronic or past infection	Exposure
IgM anti-HBc	Acute infection	Acute infection

5.5.1 Rapid field tests for HBsAg

Rapid tests that can be used in the field offer several advantages for undertaking a serosurvey: low cost; minimal training needed; laboratory infrastructure not needed; only require a drop of blood as opposed to venepuncture; no cold chain requirements; no specimen handling. They also offer immediate results with potential for counselling, referral, and immunization of contacts. However, their use in the field requires validation. A major concern is the lack of quality control procedures.

5.6 Impact of HepB introduction on the immunization programme

It may be useful to assess the impact of the addition of HepB on the NIP and the other EPI vaccines. WHO is developing a framework for evaluating the components of new vaccine introductions: vaccine selection; procurement; stocking; transport; effects on cold chain capacity (focusing especially on vaccine freezing); vaccine delivery and wastage; injection safety; record keeping; immunization coverage (administrative and surveys); staff training; acceptance by health personnel and consumers; and attitudes of political leaders and government officials.

6 ADVOCACY AND SOCIAL MOBILIZATION

Advocacy and social mobilization are perhaps the most important activities for hepatitis B control. A safe effective vaccine is available: advocacy is essential to ensure that it is offered to the entire birth cohort in every district, in every year. Social mobilization is needed to ensure that those parents ensure their children receive it.

Advocacy and social mobilization are important for immunization programmes in general, but are particularly important for hepatitis B because there is:

- no external manifestation for most infections;
- no evidence of chronic infection until a complication develops;
- an insidious onset and a very long time before onset of complications;
- a lack of recognition that HBV is responsible for the complication; and
- no directly recognizable deaths.

Advocacy is a process for raising awareness, especially among decision-makers and service providers, to ensure that the service (hepatitis B immunization) is available for all children. Increasing awareness of the importance of HBV as a cause of disease and death in the community is the key activity, and requires sound scientific data on the current and future disease burden. Another critical aspect is to show the impact of immunization in preventing that disease burden. As nearly all disease prevention will occur several decades after delivery of immunization in that cohort, special advocacy efforts are needed.

Social mobilization is the process of ensuring that parents take up an available service (hepatitis B immunization). It is similar to advocacy, but has different target audiences (primarily parents) and is focused on getting children to the point of service delivery.

For both advocacy and social mobilization, the foundation is good science and finding the effective and appropriate media to get the messages across. A range of media should be used to deliver the messages, including community volunteers and health workers, as well as the mass media. See Annex 5 for some potential advocacy messages.

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ANNEX 1

HEPATITIS B VIRUS

History

Viral hepatitis has been recognised since ancient times (the disease was described by Hippocrates). However, the different viruses that cause hepatitis have only recently been differentiated. Hepatitis transmitted through serum was first documented during a smallpox immunization campaign in 1883. McCallum proposed the term hepatitis B for 'serum' hepatitis in 1947, as opposed to the enteric-spread hepatitis A. The hepatitis B surface antigen (HBsAg) was first identified in the liver of an Australian aborigine in 1967 (initially called Australia antigen). HBsAg is the main component of hepatitis B vaccine. The immune response to HBsAg provides the basis for immunity against HBV.

Virology

Hepatitis B virus (HBV) is a DNA virus, with a core antigen (HBcAg) surrounded by a coat containing surface antigen (HBsAg). Antibody to HBcAg (anti-HBc) indicates infection- IgM if recent (usually disappears within 6 months) while IgG persists. Antibody to HBsAg (anti-HBs) only appears after clearance of HBsAg, or after immunization. The presence of HBsAg for more than six months is defined as chronic HBV infection (or carriage). The presence of a third antigen, HBeAg, indicates a high degree of infectivity (i.e. actively replicating virus).

Transmission

HBV enters the body parenterally or through small breaks in the skin or mucosal linings. The virus is found in the blood and body fluids in acute or chronic infection. Blood and fluids become less infectious as they dry on exposure to air. Most spread is between young children, probably related to contact with skin sores and small breaks in skin. The virus is also passed from mother to baby – mostly during childbirth. Sexual contact, non-sterile (shared or reuse without sterilisation) injections, and any other way of passing body fluids can lead to infection. HBV is **not** spread through air or in food. The **incubation period** before seronconversion varies from six weeks to six months and is usually three to four months.

While most spread is from child to child, the highest risk of transmission is from mother to baby. The baby of a HBsAg positive mother has a 70%-90% risk of infection if the mother is HBeAg positive, and 5%-20% risk if HBeAg negative. Immunization reduces the risk by 70%-95% – if the first dose is given soon after birth.

Hepatitis B immune globulin (HBIG) may also be given at birth to reduce the risk of infection further. However, HBIG provides only little additional protection to immunization.[1,2] Cost and supply issues create additional problems for giving HBIG. Therefore, HBIG is not an essential part of the control strategy to prevent perinatal infection.

Outcomes of infection

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

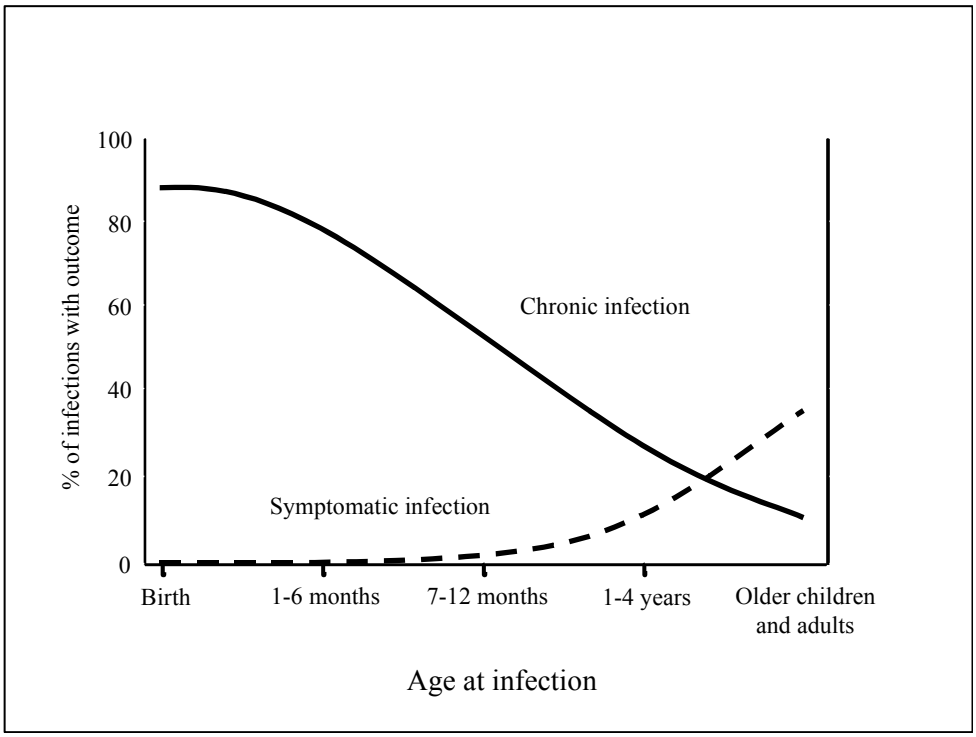
Chronic HBV infection (carriage): usually with no symptoms at the time of infection, the virus remains in the liver, where it eventually (after decades) can cause liver cancer or cirrhosis leading to premature death in up to 25% of chronically infected persons. The major HBV-related disease burden is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

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

Annex 1

The age at which a person becomes infected with HBV is the main factor determining the outcome (Figure A1). The risk of chronic infection drops from about 90% in the first six months of life, to about 25% by the age of five years, and to 10% by the age of 15 years.[3] It is unusual (2%-5%) for those infected in later adult life to develop chronic infection. Fewer than 10% of under five-year olds but 30%-50% of adults develop acute hepatitis B after infection.[4]

Figure A1. Outcome of hepatitis B virus infection by age at infection



Source: WHO/HQ guidelines

Epidemiology

In many developing countries, testing of patients with acute hepatitis is limited or not done. Therefore, accurate data on the incidence of acute hepatitis B are not available. The prevalence of chronic HBV infection, determined through prevalence studies, is generally used to describe the burden of HBV infection in a given geographic area or population.

Approximately 45% of the world's population lives in areas where chronic HBV infection is highly endemic (≥ 8% of the population is HBsAg-positive); 43% lives in areas of intermediate endemicity (2−7% HBsAg-positive); and 12% lives in areas of low endemicity (<2% HBsAg-positive).

"Escape mutants"

During the past decade, there have been occasional reports in the literature of persons infected with HBV variants and mutants. Some persons infected with HBV mutants are HBsAg negative; infection is detected with molecular techniques such as polymerase chain reaction. Even with high levels of antibody, some persons have been infected with such "escape mutants". Despite apparent increases in reports, the prevalence of HBV escape mutants is low, and it is not yet clear whether these escape mutants are of public health importance. Ongoing monitoring is needed to assess their implications.

ANNEX 2

HEPATITIS B VACCINE

History and types of vaccine

Plasma-derived HepB, available from 1982, uses HBsAg from the blood of people with chronic HBV infection. Recombinant vaccines became available in 1986, using HBsAg derived from genetically modified yeast cells (and now also mammalian cells). The gene coding for production of the HBsAg protein is inserted (recombined) into the yeast or mammal genes.

In both types of vaccines the HBsAg is joined to an aluminium salt to increase immunogenicity. The vaccine can also contain preservative (e.g. thiomerosal)

Although available only in limited supplies initially, there is now an abundant supply of recombinant HepB vaccines and these are now the most commonly used variety.

Combination DTP-HepB vaccine

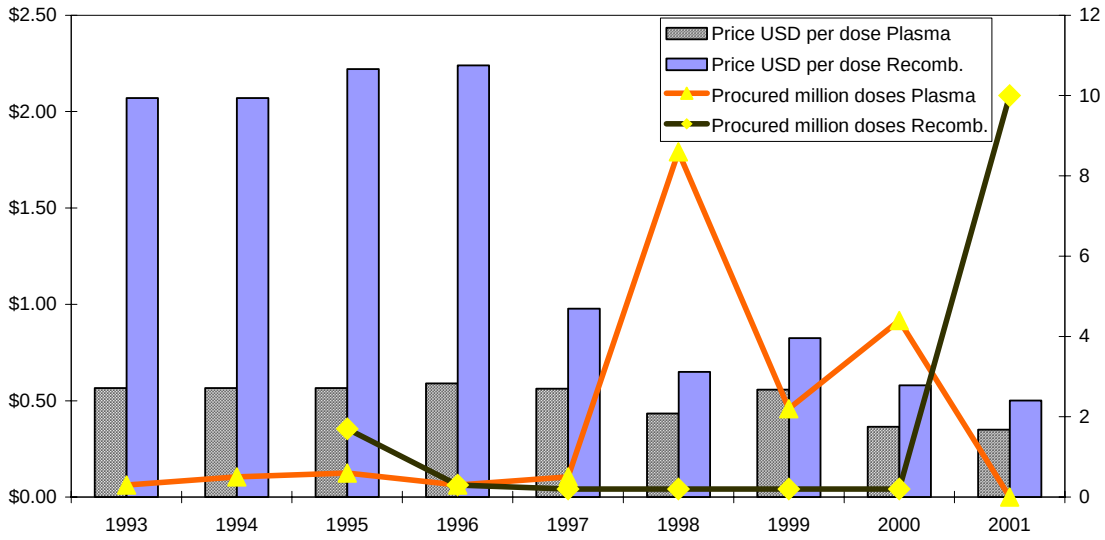
There has been considerable work done to produce a vaccine that combines DTP with hepatitis B. Although this appears to be a simple task, there are complex physical, chemical, and immunological problems that have to be resolved. At present only a single manufacturer has succeeded in bringing a combination DTP-HepB to market. That vaccine is also available as DTP-HepB-Hib.

The combination vaccine can be used instead of the separate hepatitis B and DTP vaccines, except for the birth dose, where monovalent hepatitis B vaccine must be used, because DTP is not recommended before the age of 4 weeks (see Table 1 on p. 7).

The decline in cost

A major obstacle to uptake has been cost – a three-dose course of HepB initially cost over US$100. Prices declined dramatically in the 1980s, a major factor being the emergence of developing country manufacturers. Although recombinant vaccines were initially more expensive than plasma-derived, the price differential has now virtually vanished. (Figure A2)

Figure A2. Average price and volume of hepatitis B vaccine from UNICEF, 1993-2001



Annex 2

There is a current global overcapacity to produce hepatitis B vaccine. At the same time there is a global shortage of combination DTP-HepB, which had a 2001 price of $1.10 per dose (over double the average price of monovalent hepatitis B), as there is only a single manufacturer supplying the combination vaccine.

Vaccine efficacy

Hepatitis B vaccine, both plasma-derived and recombinant, is remarkably effective. There do not appear to be important differences in the efficacy of the different types of vaccines. Clinical trials in high-risk groups have shown immunogenicity of 85%-95%, and virtually complete protection in those who developed antibody levels of ≥ 10mIU/ml (considered the protective level).

At least 95% of infants, children and adolescents develop protective antibody levels after three doses of vaccine. The response rate drops with age from 90% for adults under 40 years to about 70% for those aged 60 years. Smoking, obesity, HIV infection, and chronic disease all reduce the response rate, but age is the primary factor affecting response.

Timing of birth dose

The baby of a HBsAg positive (carrier) mother (BCM) has a 70%-90% risk of infection if the mother is HBeAg positive, and 5%-20% risk if HBeAg negative. Immunization dramatically reduces that risk, but a timely birth dose is needed. However, there are limited data on when a birth dose is too late to protect the BCM. Receipt of the first dose (less than seven days after birth) among infants of highly infectious mothers (HBeAg positive) provides higher protection (70%95%) than if given after one week (50%-57%).[1, 5-7] But none of these studies differentiated infants who received vaccine very early from those receiving it later in the first week. An exception was the protective efficacy of 75% found in one group of infants of HBeAg-positive mothers who received vaccine alone in week two.[8] Given the importance of early protection, WHO recommends a birth dose within 24 hours of birth.

Vaccine schedules

In the initial trials, vaccine was given as three doses at 0, 1, and 6 months. Hence, most manufacturers tend to recommend this schedule. However, hepatitis B vaccine has been shown to be immunogenic using a wide range of schedules.[9] In general, three doses with an interval of at least four weeks (but not more than two months between doses one and two), are recommended.

Although antibody levels decline after immunization, immune memory is maintained, and booster doses do not appear to be needed to maintain immunity, for the duration of follow-up studied up till now.[10] Therefore, booster doses are not currently recommended by WHO and other experts.[11]

Vaccine safety

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

Since its first use, there have been concerns about the potential for infection from plasma-derived vaccines. However, there is no evidence to support such concerns, and the intense purification and sterilization procedures have been proved safe to prevent transmission of blood-borne viruses such as HIV. Previous concerns about an association between HepB and an increased risk of demyelination (e.g. multiple sclerosis) have proved unfounded.

Annex 2

Availability and future supply

In 2001, UNICEF procured 10 million doses of hepatitis B vaccine (all recombinant). The available supply offered to UNICEF by manufacturers was 331 million doses of recombinant vaccine and 10 million doses of plasma-derived vaccine. The global supply is continuing to increase with the amounts offered to UNICEF in 2002 and 2003 at 426 and 531 million doses, respectively.

Six manufacturers are pre-qualified[#] recombinant vaccine producers (Green Cross (Republic of Korea), Lucky Goldstar (Republic of Korea), Merck (USA), CIGB (Cuba), GlaxoSmithKline (Belgium), and (from 2002) Shantha Biotec (India). One manufacturer, Cheil Jedang (Republic of Korea) is pre-qualified for plasma derived vaccine, though it is in the process of changing its technology to produce recombinant HepB.

Only one DTP-HepB combination vaccine is available (GlaxoSmithKline, pre-qualified). Manufacturers in Brazil, India and Indonesia are working on producing DTP-Hep B combination vaccines, but it is thought that none will be available for global purchase until at least 2004 as trials and licensing will need to be complete before the pre-qualification process can begin. In contrast to the supply of monovalent vaccine, only 10 million doses of combination vaccines were offered to UNICEF for 2002. No substantial increase in supply is likely before 2004.

Ensuring that vaccine is not frozen

Hepatitis B is very freeze-sensitive. One way to prevent vaccines being exposed to freezing temperatures is to remove them from the cold chain (in warm climates) and use vaccine vial monitors to monitor heat exposure (see 4.1.2).

To prevent freezing during air cargo, vaccine manufacturers should follow guidelines on international packaging and shipment of vaccines.[12] Temporary storage period during custom clearance should be kept to a minimum. The condition of the vaccines on arrival, including the state of freeze indicators should be assessed and recorded with every shipment.

To prevent freezing during storage in cold rooms, ensure:
1. Refrigeration units' plume of cold air close to the evaporator, has free flow
2. The evaporator is fitted with mesh cage to prevent vaccine being stored in danger zone
3. Ceiling mounted units are positioned in the centre of circulation aisles.
4. The Air outlets, in ceiling mounted units, are directed away from any shelving.
5. Alarms are fitted to continuous/intermittent recording temperature monitoring devices.

To prevent freezing during storage in cold climate:
1. Permanently heat the vaccine store
2. Heat the cold room (+2°C to +8°C cold rooms should be fitted with frost protection heater circuits, unless the space in which the cold room is housed is permanently heated and the heating system is 100% reliable.)

To prevent freezing in refrigerators:
1. Do not store freeze-sensitive vaccines within 20cm of ice-lined refrigerator's base
2. Keep the thermostat at a setting to ensure 8°C at the hottest time of the day.

[#] WHO advises UN agencies on the quality of vaccines for purchase. The evaluation process is performed according to a published procedure: "The procedure for assessing the acceptability, in principle, of vaccines for purchase by United Nations agencies" (WHO/V&B/02.08). The vaccines that fulfil, in a satisfactory manner, this evaluation process are pre-qualified for purchase by UN agencies and are put on a list, updated monthly, published on the WHO website at: http://www.who.int/vaccines-access/vaccines/Vaccine_Quality/UN_Prequalified/

Annex 2

To prevent freezing during vaccine transport:
1. Condition icepacks before loading a cold box.
2. Use cold packs (not frozen)
3. Use warm packs in extremely cold climates
4. Use heated vehicle or transport
5. Avoid the cold (do not leave the cold boxes outdoors and/or in unheated rooms)

Tools to detect freezing:
1. Continuous/intermittent temperature recording especially for storage facilities
2. Vaccine arrival report (Documenting the freeze indicators status on vaccine arrivals)
3. Freeze Watch
4. Stop Watch
5. Shake test

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ANNEX 3

STATUS OF HEPATITIS B IN WPR COUNTRIES

Table 1. National Immunization Programme (NIP) current and historic use of vaccine

Country/Area	First Year in NIP	Year recommended for infants (part or whole country)	Year routinely offered all infants	Potential for less visits	HepB1	HepB2	HepB3	Booster(s)	BCM - extra doses	Public vaccine to: School children, Health workers, Contacts, Others#	Oldest full cohort offered protection (year born)	Birth dose % given within 24h	Births % In hospital	Births % HW attended (in or out of hospital)	HBIG given to BCMs (public)
	History of NIP			Schedule - infants & use in others								Birth Dose			
American Samoa	1986	1986	1987	Y	0	1m	12m			#	1986	100	100	100	Y#
Australia	1997	2000	2000		0	2m	4m	6/12m#		S	~1984		98	99	Y
Brunei Darussalam	1983	1988	1988	Y	0	1m	6m			H,C	1988		99	100	Y
Cambodia	2001	2001	2005		6w	10w	14w						6	38	N
China	1992	1992	1992	Y	0	1m	6m				1992	80		67	N
Cook Islands	1989	1989	1989	Y	0	1m	6m				1989		100	100	Y
Micronesia, F.S.	1989	1989	1989		0	2m	6m	12m		S,H,#	~1980	80	80	90	Y
Fiji	1989	1995	1995	Y	0	2m	5m				1989	22	97	99	Y#
French Polynesia	1990	1990	1990	Y	0	1m	6m			S	~1980	97	n/a	100	Y
Guam	1989	1990	1990		0	2m	6m		#		1990	99			Y
Hong Kong (China)	1984	1988	1988	Y	0	1m	6m			S,H,O	1986	99	100	100	Y
Japan*	?	N	N		#	#	#						99	100	Y
Kiribati	1995	1995	1995		0	6w	14w				1995		32		N
Lao P.D.R.	2001	2001	2004		6w	10w	14w						11	21	N
Macao (China)	1984	1989	1989	Y	0	1m	6m	5y		S,H,#	1981		100	100	Y
Malaysia	1989	1989	1989	Y	0	1m	5m			H,#	1989	94	94	97	N
Mariana Is., Northern	1989	1990	1990		0	6w	6m			S,H,#	1983		100	100	Y
Marshall Islands	1988	1988	1993		0	2m	6m						72	85	N
Mongolia	1987	1987	1991	Y	0	2m	8m				1987	90#	99	99	N
Nauru	1983	1984	1985	Y	0	1m	6m	5y			1985		100	100	Y#
New Caledonia	1989	1989	1989	Y	2m	3m	9m		#	C,H,#	1990	100	96	96	Y
New Zealand	1985	1988	1988		6w	3m	5m		0	S,C,H,#	1984		98	99	Y
Niue	1986	1986	1986	Y	0	4w	6m			H,#	1979		100	100	Y
Palau	1988	1988	1988		6w	4m	12m		0		1988				
Papua New Guinea	1989	1989	1989		0	1m	3m			H	1989			45	Y
Philippines	1991	1992	not yet		6w	10w	14w			#	-		34	56	N
Republic of Korea	1984	1995	1995	Y	0	1m	6m				1985		98	98	Y
Samoa	1990	1990	1990		0	6w	14w				1990		80	90	N
Singapore	1985	1987	1987	Y	0	1m	5m		12m	H,C	1987		100	100	Y
Solomon Islands	1990	1990	1991		0	2m	4m				1991				N
Tokelau	1997	1997	1997	Y	0	6w	5m			#	<1997		100	100	N
Tonga	1988	1988	1988		0	6w	5m			#	1988		93	94	N
Tuvalu	1993	1993	1993	Y	0	6w	9m				1993		100	100	Y
Vanuatu	1993	1993	1993		0	6w	14w				1993		37	53	Y
Viet Nam	1997	1997	2003		0	2m	4m					32	10	70	N
Wallis and Futuna	1992	1992	1992	Y	2m	3m	9m			#			100	100	Y

**=in 3 days of birth

Y = Yes

N = No

NR = Not reported

Not applicable

BCM= Baby of carrier mother

* Japan gives only vaccine to BCMs

- See supplementary information

Annex 3

Table 2. Hepatitis B vaccine coverage, status of integration into EPI, and source

Country/Area	1995	1996	1997	1998	1999	2000	2001	HepB3 coverage close to DTP3	1999 DTP3%-HepB3%	2000 DTP3%-HepB3%	2001 DTP3%-HepB3%	HepB3 for "fully immunized child" (FIC)	Local production	Donor funding	UNICEF procurement
	HepB3 coverage(%) <1yr old							Integration					Vac. Source		
American Samoa	47	59	NR	85	91	81	98		0	4	-5			100%	Y
Australia						94	94	Y			-2	Y		0	
Brunei Darussalam	NR	NR	98	100	93s	100	100	Y	-1	-1	0			0	
Cambodia														100%	Y
China	NR	~50s	NR	NR	70s	NR	65	N	27	NR	13	Y	100%	~15%	
Cook Islands	86	65	98	86	NR	97	92		3	0	0			0	Y
F.S. Micronesia	82	86	78	79	82	97	81		-1	-2	-6	Y		100%	
Fiji	82	77	98	98	88	82	93	Y	13	NR	-3	Y		0	Y
French Polynesia	NR	79	79	94	94	97	95	Y	4	0	2			0	Y
Guam	91	87	95	94	99	99	89		-9	-7	1			100%	
Hong Kong (China)	100s	99s	99s	99s	88	88	86	Y	1	0	0	Y		0	
Japan													100%	0	
Kiribati	36	66	97	89	82	90	85		-4	0	0			0%	Y
Lao P.D.R.														100%	Y
Macao (China)	85	85	88	92	92	91	90	Y	0	1	2	Y		0	
Malaysia	87	87	89	91	91	93	94	Y	3	2	2	Y		0	
Mariana Is., Northern	94	NR	98	99	NR	89	NR	Y	3	-1	NR			100%	
Marshall Islands	47	68	70	80	80	38	NR	N	-14	15	NR			100%	Y
Mongolia	89	92	88	91	92	94	95	Y	2	1	0	Y		100%	Y
Nauru	72	90	91	90	90	45	95	Y	2	-14	0			0	Y
New Caledonia	93	95	NR	96	91	NR	NR	Y	NR	NR	NR			0	?
New Zealand	88	NR	104	87	89	90	90	Y	-1	0	0	Y		0	
Niue	90	100	100	100	100	100	100	Y	0	0	0			0	Y
Palau	100	100	90	96	96	96	NR		0	0	NR			100%	
Papua New Guinea	43	63	59	69	71	73	36	N	6	2	12			~70%	
Philippines	35	62	37	35	45	2	80	N	NR	76	-10	N		0	Y
Republic of Korea	NR	NR	85	90	87	79	83	NR	NR	4	-25	Y	100%	0	
Samoa	96	98	99	99	99	96	98	Y	-1	4	-5			0	Y
Singapore	NR	87	88	89	89	91	91	Y	-1	NR	1			0	
Solomon Islands	68	97	73	NR	NR	NR	78	Y	NR	NR	0			100%	Y
Tokelau			100	100	100	100	NR	Y	0	0	NR			0	Y
Tonga	91	94	95	96	93	97	96	Y	1	-2	-2			0	Y
Tuvalu	49	86	88	96	93	78	99	Y	-9	-3	-3			0	Y
Vanuatu	66s	69s	75s	75s	75s	75s	69	N	15	15	24			0	Y
Viet Nam			55*	69*	82*	94*	97*		10	2	1		~15%	~85%	Y
Wallis and Futuna	71	NR	82	95	NR	100	NR	Y	0	0	NR			100%	

Y = Yes
N = No
NR = Not reported
Not applicable
s = survey data, otherwise administrative
* Viet Nam coverage only in districts using vaccine (~10%)

Note: "HepB3 coverage close to DTP3" judgement by national authority.

Annex 3

Table 3. Hepatitis B seroprevalence, impact of immunization, and plans

Country/Area	Best estimate (WPRO)	WPRO estimate in 1997	Official pre-vaccine estimate	Estimate (95% CI) from available studies of pre-vaccine % HBsAg+	Representative population sample	Blood donors	Ante-natal tests	Impact of vaccine assessed	HBV carriage % change (vaccinated children)	Request help to monitor HBsAG+	Acute hepatitis B data	Acute cases % change post-vaccine	National Plan	Help requested: Advice; Review programe; National plan; Serosurvey, Training
	Pre-vaccine HBsAg+ (%)							Impact assessment						
American Samoa	7	7	7	5.7(4-7)	6			Y			Y	N	Y	T
Australia	<1	0.5									N		Y	
Brunei Darussalam	5	8		5.2(5-6)		5					Y	?	Y	S
Cambodia	9	12				9					N		Y	
China	10	12	10	11(10-11)				Y	~90%		N	NR	Y	R
Cook Islands	10	10									Y	?	Y	R
F.S. Micronesia	15	12	15		15		10	Y	~85%		N		Y#	
Fiji	11	11		10 (8-12)				Y	90%		N		Y	S,N,T
French Polynesia	3	10	3				3						NR	
Guam	4	4												
Hong Kong (China)	10	12	10				10#	Y	89%		Y	17%	Y	
Japan	2	2	2	1(0.5-1.2)		0.5		Y			Y		Y	
Kiribati	29	31		29(25-32)		15		Y	86%		NR		Y	N
Lao P.D.R.	8	12				>10	6				N		N	N
Macao (China)	11	12	11				10				Y	49	Y	A
Malaysia	5	5	3-14	5(4-6)							N		Y	T
Mariana Is., Northern	5	5									N		N	S
Marshall Islands	12	12									N		N	
Mongolia	10	14	10-39	9(7-10)				Y	~50%		Y	64%	Y	
Nauru	20		40	15(12-17)							Y	?		A
New Caledonia	6	8		9(7-10)				Y			Y	?	Y	
New Zealand	<1	1	<1	7(7-8)#	1	1					Y	~85%	N	
Niue	8		8	12(10-13)							N		Y	
Palau	20	12	20											
Papua New Guinea	8	20		7(6-8)							N		Y	
Philippines	9	10	9	8(7-8)			9				N	-	N	A
Republic of Korea	5	12		4(4-5)		7					Y		Y	
Samoa	6	8		6(4-8)									Y	
Singapore	5	12	5	5(5-6)				Y	100%		Y	~85%	Y	
Solomon Islands	21	20		21(20-23)									N	
Tokelau													Y	S
Tonga	18	20		18(15-20)				Y	66%		N		Y	
Tuvalu	15						15#				N		Y	A
Vanuatu	21	19		21(19-23)				Y	81%		N		N	S
Viet Nam	14	12	17	10(9-11)							N		Y	N
Wallis and Futuna	8	8						Y	100%				Y	A

Y = Yes

N = No

NR = Not reported # - See supplementary information

WPRO = WHO Western Pacific Regional Office

Please report any additional data on pre-vaccine seroprevalence and impact to WPRO/EPI

Annex 3

Supplementary information to data in Tables 1-3

	Vaccine use in infants	Others given (public) vaccine	HBsAg+, acute disease and Vaccine Impact	National Plan
American Samoa	BCM given HBIG within 7 days of birth; HepB3 at 6mo; tested at 12mo	All under 21 year olds; others tested then immunized if susceptible	Acute hep B shows no impact from immunization - no data provided	Health education, idenitifying cases, and testing household contacts
Australia	Two schedules (depends on vaccine used): 0,2,4,6mo or 0,2,4,12mo. Combination vaccine used in most states. No monitoring birth dose timeliness	Catch-up programme for 10-13 year old children	No comprehensive data on HBsAg prevalence; limited data show: 0.1-0.2% in Europeans; 3-9% in indigenous populations	Infant immunization and disease notification
Brunei Darussalam		Health workers. Household and other contacts of carriers		Routine EPI + antenatal and blood screening; follow-up of carriers
Cambodia	Phasing in DTP-HepB over 4 years, starting in 2001. Birth dose will be piloted in 2 places in 2002	No	HBsAg serosurvey in pilot province in 2001: 9-17mo: 3%; 4-5yr: 5%; 13-15yr: 8%; 20-35yr: 11%	National plan proposed in 2001
China	Birth dose – 80% in first 48hrs of life (1999 survey); but only 67% health worker attendance at birth (ranging from 16% in Tibet to 98% in Beijing). Policy of HBIG for BCM being considered – will not be free		9.9% HBsAg+ (40% HBeAg+) in cross-sectional national survey of 60,000; now <1% in vaccinated children	Target of >85% coverage by 2006, monitor coverage, use sero-survey and pilot acute surveillance
Mariana Is., Northern	BCM given HBIG within 12 hours of birth –all babies born in hospital	Travellers, students, health workers and police officers		
Cook Islands		Students		Routine vaccine use and increase target age group.
Micronesia, F.S.	All children born in the 4 hospitals get birth dose of vaccine within 24 hours. Policy to give HBIG to BCM, but not been available for several years. Vaccine funded by CDC USA	Health workers, student travelling abroad, adults and by request. Required for college and high school entry	2-6 yr olds HBsAg+ reduced from 15% (1988) to 2.5% (2000). Study: HBsAg+ 0% if birth dose; 5% if did not get birth dose	No formal plan, but annual grant request to CDC fills that function
Fiji	Vaccine introduced in 1989, but not well established because of cost and erratic supply until 1995 (Pacific HepB project). HBIG given since 1995, but not consistently because of cost to Govt. F$38.55	Health workers at risk of exposure	Best pre-vaccine estimate: 11% HBsAg+ (1980). 1997 study HBsAg+: 9-24mo old (vaccinated): 0.7%; 9-12yr old (unvacinated): 6.9%; mothers of infants of 6.6%	Immunization for infants and high risk groups, screen blood, test pregnant mothers
French Polynesia		Previously unimmunized 11 yr olds.	Antenatal tests (1997-99): 2.5% HBsAg+.	
Guam	BCM given vaccine at 0,1,6 mo			
Hong Kong (China)	Nearly all newborns (>99%) get birth doses before discharge from hospital, but no data on timeliness. Survey data higher than administrative data for HepB3 as latter does not include some doses given in private sector	Health worker in public service, renal dialysis patient. Since 1998, patch-up for schoolchildren aged 10 – 13 years	Pre-vaccine: 9.6% HBsAg+ (blood donors and inpatients); 2001 estimate of 8.8%. Continuing sero-surveys and follow-up studies of vaccinated babies to monitor impact. Data on acute cases available only since 1989 (one year after start of immunization)	Responsibility of scientific working group (annual report porivded)
Japan	Infant immunization only for BCM: HBIG given within 48 hr and at 2-3 mo after birth; vaccine given at time of second HBIG, seocnd dose 1mo later; third dose 3mo after first dose (HBIG and vaccine covered by health insurance since 1995)	Voluntary vaccination for non-risk population	Blood donors: 0.46% HBsAg+, and 424 acute HepB cases reported in 2000	Prevention of transmission from carrier mothers to infants since 1995
Kiribati	No data on timeliness of birth dose, but usually witihin 24 hours of birth	No	Current best estimate is 20-30%, 25% in one school	No national plan
Lao P.D.R.	Phasing in DTP-HepB over 3 years, starting in 2001.	No	Data on acute hepatitis not good.	National plan only for introducing vaccine.
Macao, SAR	Only BCMs given vaccine from 1984; all newborns from 1989; 4th dose added in 1996. HBIG for BCM within 12 hrs of birth since 1984 in public and since 1988 in private (no fees). No data on timeliness of birth dose of vaccine; but most imminized on second morning of life	Under 12yr olds; high risk groups (health worker, household contact, on haemodialysis or who need regular blood products, intravenous drug user, disabled people living in nursing homes), security force recruits, susceptible blood donors	Pre-vaccine official estimate 11% HBsAg+; now 8.5%. Acute HepB cases declined from was 24.5 (1986-1988) to 8.8 per 100,000 (1999-2000). Antenatal tests in 2001 found HBsAg+ reduced from 10%(born 1965-1971) to 5% (born 1982-86)	Integation of HepB vaccine; monitor with serosurveys in young people and children
Malaysia		Health workers at risk; IV drug users; blood donors		National plan not comprehensive, but aime to accelerate control
Marshall Islands	Birth dose given within first 8 hours in most cases	No		No national plan

Annex 3

	Vaccine use in infants	Others given (public) vaccine	HBsAg+, acute disease and Vaccine Impact	National Plan
Mongolia	Survey of infants born in 1998-1999: 97% of urban and 90% of rural infants received first dose within 4 days of birth. Schedule changed (from 0,1,6mo to 0,1,8mo) to maintain higher antibody levels	No	Pre vaccine estimates of HBsAg+: 9.8% (1978) and 14-39% (1989). In vaccinated children 6-7% (estimated 2-3 fold reduction)	Developing new infectious diseases control programme including viral hepatitis control
Nauru	HBIG given to BCM -when available,			
New Caledonia	Changed from 4- to 3-dose schedule in 1996; abolished boosters in 1998. BCM given vaccine at 0, 1, 6 mo and HBIG at birth given before leaving maternity clinic	Household contacts, health workers, renal failure and dialysis patients	75% reduction in carriage among vaccinated; infection (Anti-HBcAg) decreased from ~ 50% (born before 1990) to 8% in those born in 1991-92	Free compulsory vaccination, with plans to monitor and accelerate control; schedule and catch-up under review
New Zealand	Started in 1985 for BCM only, then babies in high risk district in 1987, then all infants (using low dose vaccine given in four doses) in 1988; full dose recombinant vaccine from 1989 (three doses). Schedule change in 1996 with HepB3 moved form 15 mo to 5mo	Household and sexual contacts. All children under 5yrs in 1988, and from 1990 all under 16yrs are eligible but not activley offered vaccine	Pre-vaccine HBsAg+: 0.4% in Europeans and 4% in Maori (adult workers); 9% in school children in high risk area. Acute hep B cases notified decreased from 600 cases in 1980s to 78 in 2000 (but earlier data may have included carriers as well as acute cases)	No formal plan – but immunization, IVDU needle programme, donor screening, and community screening in north island. Plan to monitor coverage in national immunization register
Niue		Catch-up programme for children born 1979-1985. Plumbers, hospital staff, and if prescribed by doctor		Compulsory immunisation of all infants
Palau				
Papua New Guinea	Schedule from 2,4,6 mo to 0,1,3 mo. HBIG only in some locations (no fee)	Health workers		Part of EPI plan
Philippines	Vaccine introduced in 1991, but funding only adequate for 40% of population; progressively increased but no vaccine in 1998 and 2000 due to lack of funds	When there is remaining vaccine from an open vial	Best estimate 9.2% HbsAg+ , 20.7% HbeAg+ (1984 antenatals)	No national plan. Plan to conduct serosurvey in infants
Republic of Korea	HBIG given within 12 hours of birth with first dose	No	1988 national survey: 5.6% male, 4.4% female HBsAg+. Data on acute HepB cases only from sentinel surveillance started in 1999; 410 cases identified in 2001 from sentilnel sites . Blood donor information shows 70% decline in HBsAG+ donor registered between 1983-1998 (7% to 2%)	Prevent vertical transmission and improve vaccine coverage. Plans to monitor impact using sentinel surveillance and coverage
Samoa		No.		National plan using prevention like other communicable disease control –immunize all infants at birth
Singapore	Started in1985 for BCM; for all infants from 1987	Health workers (tested first); contacts of cases	1998-99 study: HBsAg 5% in unvaccinated; 0% in vaccinated. Acute cases reduced from 243 (9.5 per 100,000 in 1985) to 46 (1.4 per 100,00 in 2000), and in under 15 yr olds reduced from 10 per year to 0	Part of EPI plan.
Solomon Islands				
Tokelau	Birth dose given in first 24 hrs	Catch up for those not covered in 1997 campaign	Serosurvey in 1999 found no cases	
Tonga		Those who migrate to USA, and Latter Day Saints Missionaries		No details
Tuvalu		No	14.5% HBsAg+ (antenatals and seafarers)	Continue and improve immunization through education programmes
Vanuatu		Catchup for 0-5 yrs for all vaccines including HepB	Best estimate from Ambae, 8.2% of 352 women HBsAg+	Part of EPI plan
Viet Nam	Birth dose to be given in first three days of life, but many births not attended in remote areas	No	Pre-vaccine survey (Thanh Ho province) found 17% HBsAg+	Action plan for introduction (2002-2006), coverage survey in 2003 to monitor impact
Wallis and Futuna Is.	HBIG (but not vaccine) given to BCM	Children born before year vaccine introduced -1992	Impact on HBsAg+: 0% under 5 yrs, 3.7% in 5-10 yrs, 3.8% in 10-15 yrs, and 8.2% in 15-20 yrs	

Annex 3

SELECTED EXPERIENCES OF COUNTRIES IN THE WESTERN PACIFIC REGION

China: the impact of user fees

Since 1991, the Ministry of Health in China has recommended routine infant hepatitis B immunization, but, unlike the other EPI vaccines, families must pay for hepatitis B vaccine. While charging for hepatitis B vaccine allowed the introduction of an expensive new vaccine, and has led to about 70% coverage nationwide, it has also resulted in wide disparities, with coverage greater than 90% in well-developed eastern provinces and less than 50% in poorer provinces, primarily in western China.

Demonstration projects in China have shown that coverage greater than 90% can be achieved in poorer areas by reducing the cost of hepatitis B vaccine. Building on this experience, China has successfully applied to the Global Alliance for Vaccines and Immunization (GAVI) to assist in reducing user fees, the goal being for fees for hepatitis B vaccine to be the same as for other EPI vaccines. A new 2001 regulation requires hepatitis B to be fully integrated into the NIP and vaccine to be provided free of charge like other EPI vaccines. Fifty percent of the funding for the 12 western provinces and official poverty counties (containing about one-third of the birth cohort) is coming from GAVI, with the other 50% from the government. For the rest of the country, funding will be the responsibility of the province government – as with other EPI vaccines. For the GAVI project, the maximum administration fee that provinces can charge for hepatitis B vaccine is 3 RMB (~$0.37) per dose (compared with 0.5-1RMB for other EPI vaccines).

The Philippines: sustainable financing: interruption in vaccine supply

In 1991, the Philippines introduced HepB into its EPI. However, funding was adequate to cover only about 40% of the country, with the aim to increase coverage annually by an additional 10% of the population. The programme began in high performing municipalities and barangays (smallest administrative level) in 1991 and expanded to other areas from 1992 to 1997. Procurement in 1998 and 2000 was cancelled due to insufficient funds. Procurement of the vaccine in 1999 was delayed and arrived only in 2001. The problems with procurement of Hepatitis B vaccine foreshadowed problems with all EPI vaccines, with no procurement of any EPI vaccine in 2001.

Pacific island countries: a model for new vaccine introduction

The Pacific Hepatitis B Project, funded by the Governments of Australia and New Zealand, integrated hepatitis B vaccine into the routine immunization programme of the 10 Pacific island countries that had not been able to reliably obtain vaccine. HepB3 coverage was around or above 80% in all countries by the end of the five-year project, while coverage for other EPI vaccines was sustained or increased. Donor funding for vaccine purchase was reduced from 100% (1995-1998) to 75% (1999) to 50% (2000). In 2001 all but one of the Pacific island countries were able to pay the full costs of hepatitis B vaccine. The success of this sustainable model for donor funding of a new intervention was due to the high level of political commitment for the programme, technical support (including training of the workforce), and the reduced price of vaccine when the countries took over funding.

ANNEX 4

HEALTH WORKER KNOWLEDGE ASSESSMENT

1. Please list the vaccines that are used in the National Immunization Programme (NIP):
2. For each vaccine [of the ones actually used]:
   2.1. what disease(s) is prevented by this vaccine?
   2.2. how many doses needed for child to be fully immunized?
   2.3. how is the injection [i.e., im/sc/id] given and in which limb/area?
   2.4. what are the contraindications [conditions when vaccine must not be given]?
   2.5. what temperature should the vaccine should be stored at?
   2.6. is it sensitive to sunlight?
3. By what age should a child be fully immunized?
4. What is a 'missed opportunity' for immunization?
5. A 2-year-old has a card that shows only these vaccines given: BCG, DTP, OPV and HepB given at age 3 months and DTP, OPV and HepB at age 6 months:
   5.1. which vaccines would you recommend for today?
   5.2. which vaccines, and how many doses of each, will the child need to be fully immunized after receiving the doses given today?
6. Are there any IEC materials available to show/give to parents?
7. If a child has one of these conditions, which vaccine would you not give:

   Fever $<38^{o}C$

   Cough

   Diarrhoea

   Premature birth

   Previous history of any convulsions

   Relative with convulsion

Score: For questions score 1 point for each correct one, -1 for each incorrect one.

Note: Questions may need to be modified for local conditions and maximum score will depend on vaccines used and policy of the country.

Acknowledgement: These questions are based on a study by Dr Fernando de la Hoz of NIH, Colombia that found health worker knowledge correlated with immunization coverage.

ANNEX 5

ADVOCACY AND SOCIAL MOBILISATION INFORMATION

What is hepatitis B?

Hepatitis B is a virus that infects the liver. The infection can cause illness (acute hepatitis B) with fever, nausea, tiredness, dark urine and yellow skin (jaundice). More seriously, the infection can lead to a person becoming chronically infected (carrier).

What does it mean to have chronic HBV infection?

People with chronic HBV infection are at increased risk of liver cancer or cirrhosis, with a 15%-25% chance of early death from liver disease. The hepatitis B virus is second only to tobacco as a cause of cancer in humans.

What is the risk of becoming chronically infected?

The risk of developing chronic HBV infection from infection drops from about 90% in the first six months of life, to about 25% by the age of five years, and to 10% by the age of 15 years. It is unusual (2%-5%) for those infected in later adult life to become chronically infected.

How is the virus spread?

The virus enters the body through small breaks in the skin. The virus is found in the blood and body fluids of an infected person. Blood and fluids become less infectious as they dry on exposure to air.

Most spread is from child to child. However, the highest risk of transmission is from mother to baby. The baby of a carrier (HBsAg positive) mother has a 70%-90% risk of infection if the mother is also HbeAg positive, and 5%-20% risk if HBeAg negative. Sexual contact, unsafe injections, and other ways of passing blood-derived body fluids can lead to infection. The hepatitis B virus is **not** spread through the air or in food.

Can hepatitis B be prevented?

Yes. A safe and effective vaccine has been available since 1982. About 95% of infants who get the vaccine will be protected. The vaccine also protects babies of HBsAg positive mothers from infection – if they get a dose within 24 hours of birth.

Vaccine reactions

Hepatitis B vaccine causes relatively few reactions, and more often in adults than children. The vaccine causes local reactions in 5%-15% and fever in 1%-6%. These reactions are hardly ever severe. The only known severe reaction is anaphylaxis (a serious allergic reaction) that occurs in about 1 to 2 people per million doses.

Possible key messages for policy-makers

"The battle against hepatitis B is winnable. If we work together we will be able to eradicate this disease from our country. This will take many years but we will succeed"

"Every 2 minutes in our Region, a person is dying from HBV-associated liver disease."

"In future, the costs for each country will escalate as treatments become available - prevention is better than cure."

Possible key messages for mothers

"Preventing hepatitis B is as easy as 1-2-3: three doses of a safe effective vaccine"

"Vaccines to combat hepatitis B are highly protective for babies, and very safe. They are among the best vaccines ever produced."

"Make sure that your baby is vaccinated at birth and receives two further doses as arranged by your health worker."