

Estimating the local burden of *Haemophilus influenzae* type b (Hib) disease preventable by vaccination

A rapid assessment tool



**DEPARTMENT OF VACCINES
AND BIOLOGICALS**



World Health Organization
Geneva
2001

**The Department of Vaccines and Biologicals
thanks the donors whose unspecified financial support
has made the production of this document possible.**

This document was produced by the
Vaccine Assessment and Monitoring Team
of the Department of Vaccines and Biologicals

*Ordering code: WHO/V&B/01.27
Printed: October 2001*

This document is available on the Internet at:
www.who.int/vaccines-documents/

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shown in Annex 6 may be requested from:**

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Acknowledgements

This document was prepared by Daniel Feikin, Orin Levine, Chris Nelson, Ezzedine Mohsni, James Watt, Jay Wenger and Ulla Kou. Field tests of earlier versions of this tool were carried out in Egypt, Iran, Jordan, Oman, Tunisia, Uganda and Yemen. Significant contributions were made by members of a working group that met at WHO Geneva to review the tool on 19-20 October 2000. The report of the meeting (Expert review of a tool for rapidly assessing *Haemophilus influenzae* type b (Hib) disease burden, Geneva, 19–20 October 2000, WHO/V&B/01.25) is available from Vaccines and Biologicals, World Health Organization and on the Internet at <http://www.who.int/vaccines-documents/DocsPDF01/www604.pdf>.

Members of the working group included the following persons: Richard Adegbola, Abdulaziz Adish, Maureen Birmingham, Thomas Cherian, Alfred Da Silva, Francois de Chabalier, Jose-Luis di Fabio, Jose-Luis Diaz Ortega, Jesus Feris, Bradford Gessner, Paul Kilgore, Keith Klugman, Ulla Kou, Y.L. Lau, Tuija Leino, Osman Mansoor, Tony Measham, Kim Mulholland, Mac Otten, Samir Saha, Mary Slack and Mark Steinhoff (chairman).

This document may be used with *Estimating the potential cost-effectiveness of using Haemophilus influenzae type b (Hib) vaccine. Field test version 1* (WHO/V&B/01.36) available on the Internet at <http://www.who.int/vaccines-documents/DocsPDF01/www654.pdf>.

Abbreviations

ALRI	acute lower respiratory infection
ARI	acute respiratory infection
CFR	case-fatality rate
CSF	cerebrospinal fluid
DTP	diphtheria–tetanus–pertussis vaccine
EPI	Expanded Programme on Immunization (WHO)
Hib	<i>Haemophilus influenzae</i> type b
ICC	intracountry coordinating committee
ICU	intensive care unit
IMCI	integrated management of childhood illness
MOH	ministry of health
PCR	polymerase chain reaction
U5MR	under-5 mortality rate
UNICEF	United Nations Children’s Fund
WHO	World Health Organization

1. Rationale for using the Hib rapid assessment tool

Prior to the introduction of the conjugate vaccine against *Haemophilus influenzae* type b (Hib) in the late 1980s, Hib was the leading bacterial cause of meningitis and one of the leading causes of bacterial pneumonia and sepsis among young children in developed countries. The burden of Hib disease has been virtually eliminated from these countries in the decade since introduction of the vaccine. Most developing countries, however, have not implemented the Hib vaccine into their routine childhood immunization schedules. Consequently, an estimated 350 000 – 700 000 children worldwide still die of Hib disease each year.

Several important obstacles have prevented most developing countries from adopting the Hib vaccine. One is the relatively high cost of the Hib conjugate vaccine series. Of equal importance is that health officials in many countries have not seen convincing evidence to illustrate that Hib disease is a major problem among children in their country. Since Hib disease is difficult to diagnose, those cases of Hib disease that are identified account for only a fraction of the true disease burden. Without recognition of the true burden of Hib disease in their country, health decision-makers will underestimate the value of Hib vaccination and will have little incentive to spend the financial and other resources necessary to introduce the vaccine.

While global and regional estimates of Hib disease burden may already be available, variations in the availability of, and access to, health services, as well as the overall level of development in the community, may lead to major differences in disease burden between countries and populations in the same region. For this reason, health decision-makers prefer local data. Several options are available for collecting this local data including population-based surveillance or other special studies of Hib disease burden. As an alternative to these options, this tool outlines a method for making a rapid estimate in countries where rigorous, long-term studies have not been done. All of these options can promote interest in and raise the awareness of Hib disease and whether the Hib vaccine should be introduced.

The main objective of this tool is to provide a methodology for countries to rapidly assess the burden of Hib disease using as much local data as possible. This document includes information on how to collect data from locally available sources and criteria for judging the quality of that data. It then details two methods for calculating the burden of Hib disease using this data. This tool was designed to allow a rapid assessment of Hib disease burden, requiring approximately 7-10 days to complete.

2. Background

2.1 Description of Hib disease(s)

Haemophilus influenzae is an important cause of morbidity and mortality from pneumonia, meningitis and sepsis among infants and young children in developing countries. *H. influenzae* is a bacterium that can be found in the upper respiratory tract of healthy persons and, in some situations, it can cause disease. *H. influenzae* is subdivided into six serotypes (a–f). In addition, many strains are non-typable. Serotype b, referred to as Hib, is the most important strain. Virtually all episodes of *H. influenzae* meningitis are due to Hib. Of children with Hib meningitis, 10–30% die, and 10–35% of the survivors are left with disabling sequelae (e.g. deafness, paralysis, learning disabilities). In addition, Hib is also the principal serotype of *H. influenzae* that causes severe pneumonia in young children. Hib pneumonia, which has a case-fatality rate of 2–25%, is 4 to 10 times more common than Hib meningitis. Hib is also a leading cause of bloodstream infections and epiglottitis, both of which may result in the death of the infected child. Other serotypes and non-typable strains most often cause otitis media in children and are important causes of disease in elderly populations. Almost all serious Hib disease occurs between one month and five years of life. Hib disease is very rare before one month of age and after the fifth birthday.

2.2 Diagnosis

Identifying the role of Hib as a cause of disease depends on laboratory diagnosis. Because Hib meningitis is the form of invasive Hib disease most easily identified in the laboratory, the calculations of Hib disease burden outlined in this tool are based on the diagnosis of Hib meningitis.

The diagnosis of Hib as the etiologic agent in a child with clinically suspected meningitis can be made in the following ways:

- Growth of Hib from cerebrospinal fluid (CSF) culture (*Haemophilus influenzae* isolated from CSF that is not serotyped should be considered Hib).
- Positive latex agglutination test for Hib from CSF.
- Purulent CSF with a gram stain showing gram negative coccobacilli.
- Growth of Hib from blood culture.

It is more difficult to identify the etiology of pneumonia. Culture and gram stain of sputum is neither sensitive nor specific for diagnosing a bacterial etiology. Blood cultures are a more accurate way to identify a bacterial agent as a cause of pneumonia, but the sensitivity of blood cultures is low. Only about 10–20% of cases of bacterial pneumonia, including those caused by Hib, yield positive blood cultures. Cultures of lung aspirates are also an accurate method for diagnosing bacterial etiologies of pneumonia. However, this procedure can only be performed on a subset of pneumonia patients and is rarely done due to its degree of invasiveness.

2.3 Hib conjugate vaccine

Hib conjugate vaccines link the Hib polysaccharide to a more immunogenic carrier protein. These vaccines are highly effective; several studies have shown >90% efficacy for preventing serious Hib infections. Many countries that have introduced Hib conjugate vaccines into their routine national immunization programme have nearly eliminated Hib disease within a few years of introduction. Hib conjugate vaccines have also been shown to be very safe for children.

Generally, infants receive 3 doses of Hib conjugate vaccine. Some vaccines, however, are highly effective after just 2 doses. Usually, infants receive Hib vaccine at the same visits that they receive diphtheria-tetanus-pertussis vaccine (DTP), so introduction of Hib vaccines does not require additional visits for vaccination. Hib vaccines can be given as monovalent or as part of a multivalent “combination” vaccine. The most commonly available combination vaccines have combined DTP and Hib in a single injection, but combinations of hepatitis HepB/Hib and DTP/HepB/Hib vaccines are also available. When such combination vaccines are used, introduction of Hib vaccine may not require any additional injections.

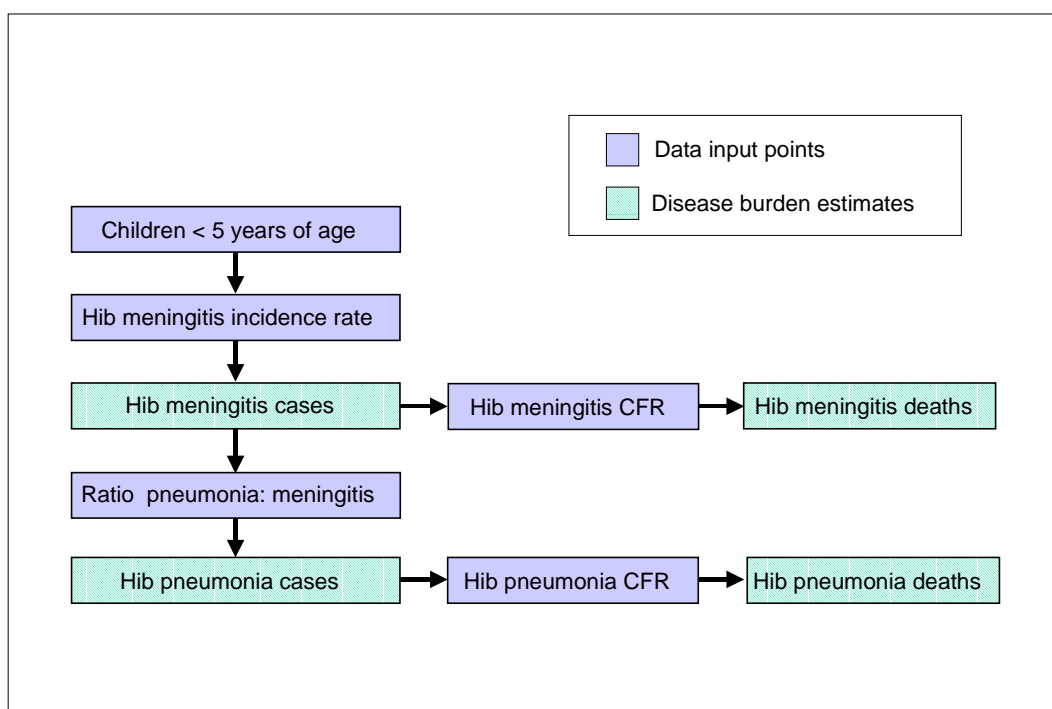
Most often Hib vaccine is simply introduced into the routine Expanded Programme on Immunization (EPI) schedule for infants. However, “catch-up” immunization of older children (e.g. <2 or <5 years old) is an option.

3. The rapid assessment method

3.1 The conceptual basis for the rapid assessment tool

This tool uses two methods to develop a national estimate of Hib disease burden with this estimate being expressed as the number of meningitis and pneumonia cases and deaths in children under five years of age that are attributable to Hib infection. The first method (“the incidence rate method”, Figure 1) uses a local estimate of Hib meningitis incidence as the basis for this calculation. The second method the U5MR (under-5 mortality rate) method,¹ Figure 2) is based on estimates of the contribution of Hib pneumonia to overall under-5 mortality. Both methods use local estimates of meningitis and pneumonia case fatality rates.

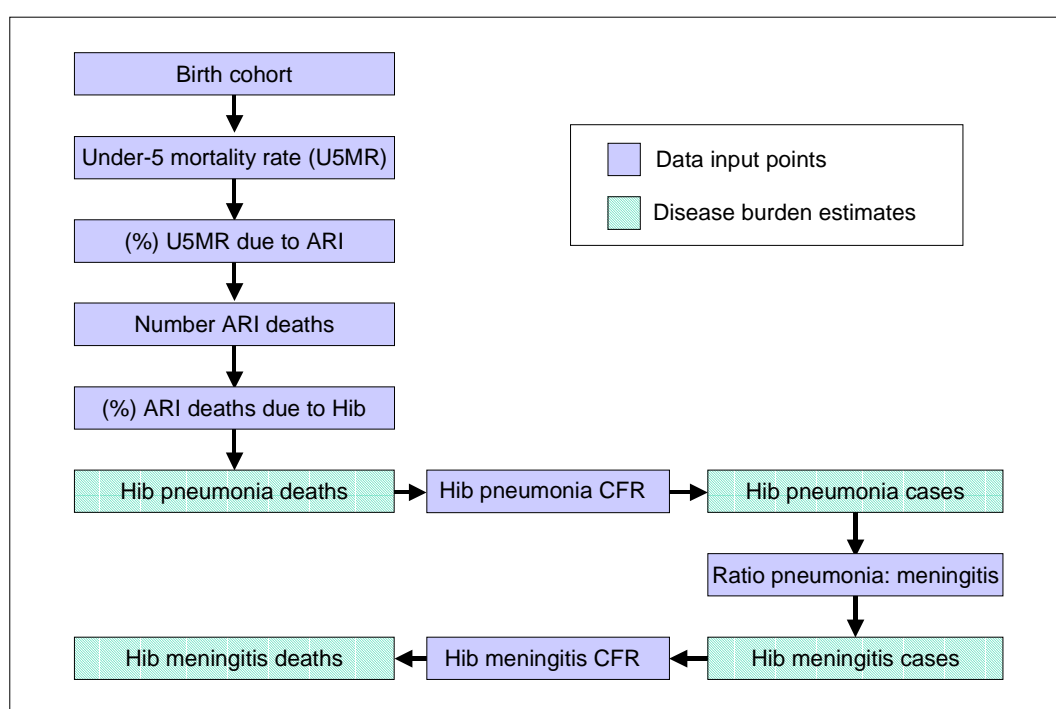
Figure 1: The meningitis incidence rate method for calculating Hib disease burden (Worksheet 2)



¹ Under-5 mortality rate. Defined as the number of deaths among children less than 5 years of age divided by the number of live births.

To facilitate the calculation of burden estimates three Microsoft Excel Worksheets are provided. Worksheets 1 and 2 support the incidence rate method. Worksheet 1 uses local data to calculate an incidence rate of Hib meningitis. Worksheet 2 calculates projections of the national burden of Hib disease using the estimate of Hib meningitis incidence from Worksheet 1 together with other inputs such as the local case fatality rate for hospitalized meningitis and pneumonia. Worksheet 3 supports the U5MR method. Both methods calculate estimates of Hib disease burden expressed as the annual number of cases and deaths due to Hib meningitis and pneumonia in children <5 years of age.

Figure 2: The under-5 mortality rate method for calculating Hib disease burden (Worksheet 3)



3.2 Managing a rapid assessment process

The value of this rapid assessment tool is as much in the process of engaging local clinicians, epidemiologists and laboratory technicians to collect, synthesize and evaluate the existing local data as in the actual estimates themselves. Making the most of this process requires efficient management of the time spent in the field. The annexes include several checklists and forms to help you manage the process as efficiently as possible. To aid in the initiation, conduct and reporting of the results of a rapid assessment process we have included a chronology of a typical visit and templates for a letter of introduction, a log of persons contacted and an executive summary of the assessment. Using these tools can help make the rapid assessment tool more efficient and more valuable.

3.3 Collecting the data to use in the rapid assessment tool Worksheets

To estimate Hib disease burden, several sources of data will be used. Often the data can be obtained from more than one source, in which case the consultant will need to assess whether the most accurate figure comes from one source or from an averaging of the figures obtained from various sources. Data is more accurate when derived from a measurement than from an interview, with more current and comprehensive data being more helpful. Asking questions in several different ways and of independent sources can help to increase the accuracy of interview data.

Documenting the source of the data is an important part of this process. It is essential that the source of all estimates or data be noted so that it can be re-confirmed at a later point, if needed. Also, the ultimate users of the estimates generated by the tool will want to know the sources of data so they can evaluate their reliability. Whenever possible, it is useful to photocopy the data sources (e.g. log book pages, manuscripts, tables, publications, etc.). Careful documentation will make the estimates more interpretable and give added credibility to the process.

Immediately following is a listing of the most important sources of data that are needed to complete the Worksheets in this rapid assessment tool. A detailed checklist of information to be gathered from each source of data is provided in Form B.

- 1) Ministry of health (MOH). Personnel of primary interest in assessing Hib disease burden include the officials involved with the EPI, surveillance of childhood or communicable diseases (particularly meningitis and pneumonia) and laboratory surveillance systems. Direct interviews with these officials are important in gathering much of the information. Interviews also establish a working relationship with the officials in the MOH who will most likely be involved in the decision to adopt Hib vaccination and its subsequent implementation. If the officials in the MOH are unable to provide some of the required data they may be able to direct you to any pertinent literature, national health statistics and other relevant sources of information.
- 2) Literature review should include all regional and international medical journals. Unpublished dissertations or theses can also be an important source of data in many countries. One of the easiest ways to identify this literature is to ask leading paediatricians, especially those in university hospitals, if they or their colleagues have written any articles on the subjects of bacterial meningitis and pneumonia. All available articles on the local epidemiology or clinical features of bacterial meningitis and pneumonia should be reviewed with special attention being paid to epidemiologic and laboratory methods.
- 3) National health statistics may be available through the MOH or the national institute of statistics.
- 4) Hospitals in urban areas will tend to have the best microbiologic resources. Public and university-affiliated hospitals may provide the most reliable and easily obtainable data on the major causes of bacterial meningitis and pneumonia, and the outcomes of patients with meningitis and pneumonia. Private hospitals also serve a substantial part of the population in the urban areas of some countries, and may also provide useful data. It should be noted though that the private hospital patients are going to represent a relatively more affluent segment of the population than the patients of public/university hospitals.

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- 5) Regional hospitals will provide more relevant data on the causes of bacterial meningitis and pneumonia for outlying parts of the country. Again, MOH officials can provide recommendations of regional hospitals that have complete paediatric and microbiology services and fulfil most of the criteria outlined in Form A.
 - 6) Several sources of relevant data may be available before you visit the country. WHO (<http://www.who.int/vaccines-documents/DocsPDF00/www542.pdf>), UNICEF (<http://www.unicef.org/statis>), the United Nations Development Programme (<http://www.undp.org/popin/wdtrends/p98/fp98.htm>) and the Demographic and Health Surveys (<http://www.measuredhs.com/>) have internet sites that contain estimates of vaccination coverage, infant and child mortality rates, and other general health information. The data available from these and other sources should be compared with data obtained locally through this rapid assessment process.

4. Using Worksheet 1: retrospective estimation of the local incidence of Hib meningitis

4.1 The importance of calculating an accurate Hib meningitis incidence rate

An accurate estimate of the Hib meningitis incidence rate is important for an accurate measure of the total burden of Hib disease. This tool provides a methodology for accurately estimating the Hib meningitis incidence rate (see Worksheet 1), which in turn is important for accurately projecting the national Hib disease burden (see Worksheet 2). The incident rate can also be used to compare the relative burden of Hib disease between different countries. Population-based studies of the incidence of Hib meningitis have been performed in many countries and, for many regions, reliable estimates of Hib meningitis rates exist for purposes of comparison (Table 2). Because the incidence rate of Hib meningitis is standardized to a population of 100 000 children less than five years of age, comparisons can be readily made between countries of differing size.

4.2 Selecting an appropriate site for retrospective calculation of Hib meningitis incidence

Incidence rate calculations require a numerator and a denominator. To estimate the incidence rate of Hib meningitis, an area should be selected where both the numerator and denominator can be obtained accurately. A checklist of the important criteria for selecting an area to calculate the incidence of Hib meningitis is presented in Form A.

An accurate numerator should include all cases of Hib meningitis that occur among children less than five years of age residing in a specified area during a specified period of time.

An accurate denominator should include all children less than five years of age residing in the same area during the same period of time.

An ideal setting would be a relatively isolated region with well-defined borders in which all children with potential meningitis would be brought to a small number (no more than three) of regional hospitals and where few children die at home without first obtaining treatment at a hospital. These hospitals should routinely obtain cerebrospinal fluid from patients with suspected meningitis and have the clinical and laboratory capabilities to determine the major causes of meningitis, including Hib. Because of potential variations in different parts of a country, two such areas should be selected for study, if possible.

National surveillance data may also help in the selection of an appropriate area for calculating Hib meningitis incidence. Passive reports of Hib meningitis generally underestimate the incidence. If passive surveillance data identifies one region as having more reported Hib meningitis than other regions of the country, then this region may represent an area with the least underreporting and the best laboratory resources. You may want to consider such a region, provided that it fulfils the other criteria outlined in Form A.

4.3 Case definitions for retrospective calculation of the incidence of Hib meningitis

For calculating an incidence rate, only patients who meet all criteria for inclusion in the numerator should be included. In some countries, regional hospitals that can identify Hib meningitis may not exist. In these countries, large hospitals in the major cities may be the only ones that effectively identify Hib meningitis. Because these are often referral centres, many children with Hib meningitis may reside outside of the city where the hospital is located. To estimate an accurate denominator for the calculation of a Hib meningitis incidence rate using a large urban hospital, it may be possible to identify the principal catchment area of the hospital and determine the population of children less than five years of age living in this area. Once this area is defined, it will be important to identify the residence of each case of Hib meningitis. Only cases who reside in this defined area should be included in the numerator.

Another important issue in calculating the Hib meningitis incidence rate is the exclusion of neonatal meningitis cases. Meningitis in neonates tends to be caused by different pathogens than meningitis in older infants and children. Hib meningitis is rare in neonates. If possible, cerebrospinal fluid from neonates (0-1 month old) should be removed from the count of purulent meningitis cases.

Ascertainment of the number of cases of purulent meningitis in any hospital will require meeting both the paediatric and microbiology services. Information to be obtained from the paediatric and microbiology visits is outlined in Form B. It is very important to review primary data, such as logbooks and medical records, when counting cases of Hib meningitis. Cross-checking of patient names and hospital numbers obtained from different sources is important to identify all unique cases of Hib meningitis. In counting cases of purulent meningitis, be careful not to double-count patients who received more than one lumbar puncture for the same episode of meningitis. Also, when reviewing clinical diagnoses of meningitis, it should be considered that Hib meningitis may be categorized as another diagnosis, such as encephalitis and meningoenzephalitis, depending on local definitions of disease.

To estimate a complete numerator you must be able to identify all potential cases, and there may be more than one hospital that potentially attends children with meningitis in the defined area. It is essential to visit all hospitals in an area that may treat childhood meningitis so that an accurate numerator of Hib meningitis cases can be obtained. If these other hospitals treat childhood meningitis but cannot isolate Hib, information from a hospital that did effectively culture Hib may be applied. For instance, the proportion of purulent meningitis due to Hib found on review of microbiologic data from a large, urban hospital may be applied to other hospitals that could identify purulent CSF but were unable to culture Hib effectively. Note that particular caution should be taken when applying the percentage of culture-positive meningitis due to Hib from a hospital that does not treat neonatal meningitis to one that does, and vice versa.

A sheet to help keep track of all potential cases of Hib meningitis is provided as Form C. You can use this sheet to make a line-listing of all cases. The bottom of Form C has a place to tally numbers that will be used in Worksheet 1. Worksheet 1 provides a step-by-step approach to calculation of the incidence rate of Hib meningitis using locally available data. This Worksheet can be used to estimate the number of Hib cases that were not laboratory-confirmed (i.e. purulent meningitis with no growth in CSF and clinical meningitis without lumbar puncture).

5. Using Worksheet 2: estimating the national burden of Hib disease based on the incidence of Hib meningitis

Use Worksheet 2 to project the national burden of Hib disease based on estimates of the local incidence of Hib meningitis. The data inputs needed to do the calculations for this method are defined below. The potential sources for these data are outlined in Table 1.

- 1) Number of children <5 years old – if this is not available, you may consider multiplying the annual number of surviving infants by five.
- 2) Incidence rate of Hib meningitis – this is the annual number of cases of Hib meningitis per 100 000 children less than five years of age. This should be obtained from Worksheet 1. However, if a local estimate of Hib meningitis incidence cannot be made, an estimate from a nearby country can be used (see Table 1 for examples).
- 3) Hib meningitis case-fatality rate (CFR) – this is the proportion of children with Hib meningitis who die from the infection. In selecting a local hospital to obtain this data, most of the hospital and laboratory criteria outlined in Form A should be fulfilled. In particular, the reliability of the calculated CFR may be questioned if any of the following indicators are found:
 - >20% of childhood deaths occur outside of the hospital;
 - lumbar puncture is not done on all suspected meningitis cases;
 - all abnormal CSF is not cultured;
 - <25% culture-confirmed bacterial meningitis cases in children <5 years old are due to Hib. (If local data is not available, an estimate from Table 1 can be used).
- 4) Ratio of Hib pneumonia to Hib meningitis – this is the number of Hib pneumonia cases that are expected to occur for each Hib meningitis case. Based on data from two clinical trials, we suggest using a ratio of 5 Hib pneumonia cases to each Hib meningitis case. Because this number can only be measured in detailed clinical vaccine trials, local data will not be available.
- 5) Hib pneumonia CFR – this is the proportion of children with Hib pneumonia who die from the infection. The CFR will vary according to whether children are treated with antibiotics. The U5MR serves as a surrogate marker for access to care (and antibiotics) in a country. Therefore, we have suggested Hib pneumonia CFR's based on a country's U5MR (Table 2).

Table 1: Sources of local data for calculating Hib disease burden, including expected range of values.

Data	Ministry of Health	Literature review	National health statistics	Major urban hospitals	Regional hospitals	Expected range
Under-5 mortality rate method						
Annual number of live births	x		x			Varies
Under-5 mortality rate	x	x	x			20-250
Proportion of under-5 deaths due to acute lower respiratory infection (ALRI)	x	x	x			10-25 ²
Proportion of ALRI mortality due to Hib	Estimates based on intensive, special studies. Generally not available from existing local data.					13
Hib pneumonia case-fatality rate		x ¹		x ¹	x ¹	5-20 ²
Hib meningitis incidence rate method						
Hib meningitis incidence	x	x				15-60 ³
Hib meningitis CFR		x		x	x	10-40
Ratio of Hib pneumonia: meningitis	Estimates based on controlled vaccine trials. Not available using existing local data					5:1

¹ Most likely only bacteraemic Hib pneumonia CFR will be available unless studies include other diagnostic techniques, such as lung puncture or antigen testing. See section VI for explanation.

² See Table 2.

³ Rates may be higher in select subpopulations (i.e. Australian aborigines). Rates may be lower in some Asian countries.

If local data is used to estimate Hib pneumonia CFR, care must be taken in selecting the appropriate value. Because the diagnosis of bacterial pneumonia is difficult to make, cases of Hib pneumonia will most likely be identified by positive blood cultures. In children, only 10–20% of patients with Hib pneumonia will have a positive blood culture. Also, bacteraemic pneumonia generally has 2–3 times higher mortality rate than non-bacteraemic pneumonia. Therefore, the CFR obtained from a series of bacteraemic Hib pneumonia cases should be divided by a factor of 2–3 to obtain the true CFR for all Hib pneumonias. The reliability of the calculated Hib pneumonia CFR may be questioned if any of the following indicators are found:

- >20% of childhood deaths occur outside of the hospital;
- blood cultures are taken from <80% of children hospitalized with pneumonia;
- <10% of bacteraemic pneumonias in children <5 years old are due to Hib.

Data on the mortality associated with severe pneumonia from the national integrated management of childhood illness (IMCI) programme or acute respiratory infection (ARI) control programme or the CFR for hospitalized pneumonia cases can also be used to estimate the Hib pneumonia CFR. Because these data do not specifically assess pneumonia due to Hib, they should be carefully evaluated using the values provided in Table 2.

Table 2: Percentage of the under-5 mortality rate (U5MR) due to ARI and the Hib pneumonia case-fatality rate (CFR) based on the U5MR.

U5MR	% U5MR due to ARI ¹	Hib pneumonia CFR (%) ²
>150	25	20
75-149	25	15
25-74	20	10
10-24	15	5
<10	10	5

¹ From Garenne 1992.

² Based on literature review of CFR in bacteraemic and non-bacteraemic pneumonias in children treated and not treated with antibiotics.

6. Using Worksheet 3: estimating the national burden of Hib disease based on the under-5 mortality rate

Use Worksheet 3 to estimate of the national burden of Hib disease from the under-5 mortality rate and the proportion of under-5 deaths likely attributable to Hib pneumonia. The data inputs needed to do the calculations for this method are defined below. The potential sources for these data are outlined in Table 1.

- 1) Annual number of live births – this may sometimes be referred to as the “birth cohort”.
- 2) Under-5 mortality rate (U5MR) – the U5MR is the number of children out of every 1000 live births who die before they reach 5 years of age.
- 3) Neonatal mortality rate – this is the number of deaths per 1000 neonates. Neonatal deaths are considered to be those that occur during the first month of life. The neonatal mortality rate will be subtracted from the under-5 mortality rate because neonatal deaths are unlikely to be due to Hib (WHO Young Infants Study Group 1999).
- 4) Proportion of childhood deaths due to acute lower respiratory infection (ALRI) – this is the proportion of deaths in children less than 5 years of age attributed to ALRI. This can be estimated based on a country’s U5MR (Table 2, Garenne 1992).
- 5) Proportion of ALRI mortality due to Hib – this is the proportion of all ALRI deaths in children less than 5 years of age attributable to Hib. This number is very difficult to calculate using local data. Based on a review of several different studies, we suggest using 13%.
- 6) Hib pneumonia CFR – this is the proportion of children with Hib pneumonia who die from the infection. See description under meningitis incidence method section above and Table 2.

7. Interpreting the estimates calculated using the rapid tool

7.1 Comparing the results obtained by each method

After collecting all of the local data available and using the Worksheets provided, the tool will provide two estimates of the national burden of Hib disease in children. Because the two methods may give different estimates, it is important to understand the strengths and limitations of each method. When an accurate local estimate of the Hib meningitis incidence rate is available, the incidence rate method provides a reasonably accurate estimate of the burden of Hib meningitis.

The estimation of Hib pneumonia burden is more complex. Because there is more uncertainty about estimating the Hib pneumonia burden than the Hib meningitis burden when using the meningitis incidence rate method, the U5MR method is valuable because it provides a second approach to estimating pneumonia burden. The two methods should provide a reasonable range for the true Hib pneumonia burden. It should also be noted that extension of the U5MR method to estimate Hib meningitis burden requires additional assumptions. The Hib meningitis burden estimated by the U5MR method may therefore be less reliable than that estimated by the meningitis incidence rate method and should be interpreted with caution. If the meningitis burden figure estimated using the U5MR method seems unreasonable, it should be ignored.

7.2 Reliability of data and sensitivity analysis

It should be remembered that the disease burden estimates from this tool are an approximation of the true figures. They should therefore be presented carefully, emphasizing that they are estimates, not exact measurements. The estimates may then be compared with values from other countries to assess their accuracy. It may also be appropriate to provide a range of possible burden estimates when reporting the results of the tool.

The expected range of values for each data point presented in Table 1 can be used to check the accuracy of locally obtained data. When a local estimate is outside the range of expected values, it may indicate that the local data are unreliable. The measurements obtained by local data can also be compared to other estimates from countries in the same region with similar health status. In general, the values obtained from local data should not vary by more than 20% from other regional estimates.

As local data are collected, the possible biases of each data point should be considered. These biases may influence the calculation of disease burden. One example of a bias due to data collection would be the undercounting of childhood deaths in rural areas. This would lead to a lower U5MR than is actually the case in the country. A further example of a bias in data collection would be the situation where lumbar punctures are only done on sicker patients; because these patients might be more likely to die, the Hib meningitis case fatality rate could be overestimated. There may be other biases in collecting local data unique to each country or hospital. After using the Worksheets to calculate the Hib disease burden, the values used for each data point should be varied to account for potential biases. This is called a sensitivity analysis. By doing this analysis a range of plausible disease burden estimates will be produced for the particular country being assessed.

8. Presenting the results of the rapid assessment process

The purpose of the rapid assessment process is to collect information that will be used by decision-makers. The estimates developed in this process should serve as the evidence base for an informed decision regarding the introduction of Hib conjugate vaccine into the routine immunization system. To help present the results effectively, a sample of an executive summary document is included in Annex 4.

8.1 Estimating the potential impact of a Hib vaccination programme

The introduction of Hib vaccine into the routine immunization system should lead to a substantial decrease in the incidence of Hib disease but its impact will depend in part on vaccination coverage. When presenting the results of this process it may be useful to provide some projections of the impact a Hib vaccination programme can have on the local burden of Hib disease. The impact of vaccination on the disease burden estimated in Worksheets 2 and 3 can be calculated by simply substituting a smaller susceptible population (see calculation below) for the original population used in step 0 of either Worksheet, which was assumed to be completely susceptible to Hib disease prior to the introduction of Hib vaccine.

$$\text{Susceptibles} = (\text{Birth cohort}) \times (1 - (\text{DTP3 coverage})) \times (\text{vaccine efficacy of 3 doses, 95\%})$$

The difference between the original disease burden estimate and the smaller estimate is the expected impact of the Hib vaccination programme. This difference can be expressed as an absolute decrease in the number of Hib cases and deaths, or as a relative decrease in the number of Hib cases and deaths, i.e. a per cent decrease (see below).

an absolute difference (n number of cases or deaths), e.g.

- Hib related cases with *no* vaccination
- Hib related cases with vaccination
- = an absolute reduction of *n* Hib related cases
(this can also be done for deaths); or

a relative difference (xx percent of cases or deaths), e.g.

- (Hib-related cases with *no* vaccination
- Hib-related cases with vaccination)
- ÷ Hib-related cases with *no* vaccination
- = a relative reduction of *xx%* in Hib related cases
(this can also be done for deaths).

9. Summary

Hib is an major cause of meningitis and pneumonia in many countries. This tool provides a rapid and inexpensive methodology for estimating Hib disease burden. These estimates of Hib disease burden can then be used by countries to evaluate the potential benefits of Hib vaccine introduction. The process of conducting a rapid assessment can also raise awareness of the importance of Hib as a childhood pathogen. Use of this tool can provide useful and timely local data for decision-making.

Table 3: Incidence rate of Hib meningitis in children <5 years of age from population-based studies in regions other than North America and Europe.

Region and country	Year	Hib meningitis cases per 100 000 children <5 yrs	Reference
Africa			
The Gambia	1985-87	60	Bijlmer et al 1992
Niger	1989-95	53	Campagne et al 1996
Senegal	1970-79	51	Cadoz et al 1981
South Africa	1991-92		Hussey et al 1994
Blacks		50	
Whites		25	
Asia			
Fiji	1990	25	Levine et al 1998
Hong Kong	1986-90	3	Lau et al 1995
China (Hubei district)	1990-92	10	Yang et al 1995
Malaysia	1985-87	8	Choo et al 1990
New Caledonia	1988-91		Anglaret 1993
Caucasian		10	Carroll et al 1993
Melanesian		70	
Vanuatu		163	
Philippines	1994-96	95	Limcangco et al 2000
Middle East			
Israel	1984-88		Halfon-Yaniv et al 1990
Bedouins		22	
Jews		22	
Qatar	1987-89	16	Novelli et al 1989
South America			
Argentina	1985-92	17	Levine et al 1998
Brazil	1991	24	Freitas et al 1993
Chile	1985-87	25	Ferreccio et al 1990

10. WHO reference documents

WHO-recommended standards for surveillance of selected vaccine-preventable diseases. Geneva, World Health Organization, 1999 (unpublished document WHO/EPI/GEN/98.01 REV.1; available from Vaccines and Biologicals, World Health Organization, 1211 Geneva 27, Switzerland or on the Internet at <http://www.who.int/vaccines-documents/DocsPDF/www9742.pdf>).

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Annex 1:

The chronology of a typical rapid assessment tool process

Although the length of each visit will vary depending on the size of the country and the number of facilities to be visited, the following will provide an approximate timeline of activities for preparing and completing the visit. It is important to inform all persons contacted during the assessment of the specific purpose of the visit. Emphasizing that the visit is about primary data collection in the field, rather than a general review of procedures and facilities, should help make the visit more efficient.

Several weeks to one month before the assessment.

Send the following materials to the point of contact in the MOH

- The cover letter provided in Annex 2.
- The Hib disease burden rapid assessment tool.
- The criteria for selecting a region to visit (Annex 5: Form A).
- The questions to be answered by MOH and contacts in hospitals (Annex 5: Form B).

Follow this with a phone call to the MOH contact person. During the call, review specific activities that should be completed in preparation for the visit and draft a provisional itinerary for the visit. Discussion points include:

- Review of meningitis and specifically Hib meningitis surveillance conducted by the MOH.
- Identification of at least 2 regions to be visited (Annex 5: Form A). Sometimes the selection of regions will be difficult from a distance. The regions selected can be reviewed and further discussed once you arrive in the country. Make sure you communicate that you are not looking for a region with a “model” hospital or surveillance system, but one that meets the criteria necessary for the tool.
 - Distribution of Annex 5: Form B questions to appropriate people within the MOH and regional hospitals. The cover letters in Annex 2 may also be sent to regional hospitals ahead of time.

During the assessment,

spend one to two days visiting the national MOH.

- Review meningitis and specifically Hib meningitis surveillance conducted by the MOH.
- Review the regions chosen for the assessment (Annex 5: Form A) and contact the appropriate people at the regional MOH and hospital paediatric and microbiology services to reconfirm the visits. If the regional people have not already received the appropriate sections of Annex 5: Form B and cover letter explaining the visit, send this information immediately (i.e. fax, direct delivery or reading them over the phone if necessary).

spend one to two days per hospital visit.

- Meet regional MOH representatives and discuss questions assigned in Annex 5: Form A.
- Meet chief of paediatric services from regional hospital
 - Discuss questions assigned in Annex 5: Form B
 - Identify at least a 12-month time period for review
 - Using Annex 5: Form C, make a line listing of all cases of meningitis in children <5 years of age.
- Meet chief of microbiology lab in the regional hospital
 - Discuss questions assigned in Annex 5: Form B.
 - Using the same time period defined in the paediatric service visit, use Annex 5: Form C to make a line listing of all cases of Hib identified in CSF and blood in children <5 years of age.
- Using the data in Annex 5: Form C, link patients identified in the paediatric service and laboratory visits.
- Hospital records
 - Verify the clinical diagnosis of any cases that might be Hib meningitis (i.e. blood culture positive for Hib, clinical meningitis caused by unknown agent).

spend one to two days calculating Hib disease burden and writing the trip report.

- Calculation of incidence rate of Hib meningitis using Worksheet 1.
- Use Worksheets 2 and 3 to calculate Hib disease burden nationally.
- Write the executive summary (Annex 4) and trip report with conclusions and recommendations.

spend one day debriefing with the MOH and other interested parties.

Annex 2:

Letter of introduction from consultants to the MOH or facilities, to be sent prior to visit

Dear Dr _____ :

As discussed, we will soon be visiting *country or facility name* to assist the Ministry of Health in assessing the burden of severe disease caused by *Haemophilus influenzae* type b (Hib) among young children. The proposed dates of our visit will be *dd.mm.yy – dd.mm.yy*. The objective of our visit will be to collect as much local data as possible in an effort to calculate the number of cases and deaths due to Hib meningitis and Hib pneumonia occurring annually in your county in children less than 5 years of age. This information should prove useful in assisting your country in deciding whether to adopt the Hib vaccine at a national level. This is not an audit or critical review of surveillance systems or clinical/laboratory facilities and this should be emphasized to all parties who will be contacted during our visit.

The following is a suggested itinerary for our visit to your country, although the structure of the visit is flexible:

- | | |
|----------|--|
| 1-2 days | Meet with national Ministry of Health officials, specifically the director of communicable disease surveillance and/or the EPI manager. |
| 2-5 days | Visits to hospitals in the capital and at least 2 regions. We would like to meet with the chiefs of the paediatric services and the microbiology lab at each hospital. |
| 1-2 days | Calculation of disease burden estimates and report writing. |
| 1 day | Presentation of findings to the Ministry of Health and any other interested parties. |

We are sending several documents to help us prepare for the visit. Annex 5: Form B has a list of questions, some of which can be answered prior to our arrival. We are sending these questions so that you will have some time to gather the type of information that we will need to do our assessment. The first section should be filled out by you at the national Ministry of Health. The other sections can be sent to officials in the regional Ministry of Health offices and regional hospitals.

We are looking to visit hospitals that treat children with bacterial meningitis, in particular those hospitals that have the microbiologic capacity to isolate Hib from the cerebrospinal fluid. An essential part of our visit will be the calculation of an annual incidence rate for Hib meningitis per 100 000 children <5 years of age.

An ideal setting for calculation of an incidence rate would be a relatively isolated region in which all children with potential meningitis would be brought to one regional hospital and where few children die at home without first obtaining treatment at a hospital. The regional hospital should routinely obtain cerebrospinal fluid from children with suspected meningitis and have the clinical and laboratory capabilities to determine the major causes of meningitis, including Hib. A more detailed list of the criteria important for finding an appropriate region is provided in Annex 5: Form A.

Please consider which regions of your country may be appropriate for calculation of an incidence rate. If you identify such regions, please arrange for our visit to the regional hospital and send ahead the appropriate questions provided in Annex 5: Form B. However, if regional hospitals in your country do not culture cerebrospinal fluid for Hib, we may still be able to use the rapid assessment tool in hospitals in large cities. We can discuss the selection of the best areas to do the rapid assessment by phone or upon our arrival. We have found it very useful to inform the individuals we will meet about the reason for our visit well ahead of our arrival and to send them a questionnaire (Annex 5: Form B) indicating the type of information we will be looking for. This will make for an efficient and cooperative visit.

We would like to contact you by phone or email sometime in the week before our visit to address any last minute details or questions. If you need to reach us for any reason, please feel free to do so. Thank you very much for your time and work and we look forward to seeing you soon.

Yours sincerely,

[Your name and affiliation here]

Annex 3:

A log of persons contacted during the assessment

National level contacts

WHO country personnel

Name *WHO Representative*

Contact information:

Mailing address:

Cell phone:

Office phone:

Office fax:

Office e-mail:

Name *WHO EPI Personnel*

Contact information:

Ministry of Health

Name *Title*

Contact information

Provincial level contacts

Name *Title*

Contact information

District level contacts

Name *Title*

Contact information

Annex 4:

An executive summary of the rapid assessment findings and recommendations

This template is designed to help you effectively communicate the main findings and recommendations of the rapid assessment process to the decision-makers in the country who will be involved in the decision to introduce Hib vaccine. The executive summary document should not exceed 2 or 3 pages in length. The outline below can help to get across many of the key points in a concise manner.

- Current situation with Hib disease
 - global situation: invasive Hib disease as a cause of morbidity and mortality among children
 - number of countries currently using Hib vaccine in routine EPI programme in the region
 - current knowledge of Hib burden in *country*
 - status of Hib vaccine use in the private sector
 - status of current efforts to define the burden of Hib disease in *country*
 - description of meningitis surveillance and how it is related to Hib burden.
- Terms of reference for the visit
 - estimate the burden of disease attributable to Hib infection using the WHO rapid assessment tool for estimating the local burden of *Haemophilus influenzae* type b (Hib) disease
 - evaluate laboratory capacity for conducting sentinel surveillance of invasive Hib disease in the community.
- General Description of field activities
 - regions chosen for the assessment, reasons for choosing these regions, MOH offices and facilities visited and description of activities at each visit.
- Summary of clinical and laboratory findings
 - summarize clinical findings including number of Hib meningitis cases, case fatality rate, and estimated incidence of Hib meningitis from Worksheet 1 (may be presented in table as shown below for a hypothetical country)
 - summarize laboratory capacity for culturing *Haemophilus influenzae*
 - summarize disease burden results from Worksheets 2 and 3 (subnational and national estimates may be presented in table as shown below for a hypothetical country).

**Hib meningitis incidence and case fatality rate
among children, *Country (date)*.**

District	Hib meningitis		Assessment period	Facility
District X	Number cases	38	May 1999 – November 2000	Hospital A
	Incidence ¹	7.1		
	Case-fatality	25%		
District Y	Number cases	21	October 1999 – October 2000	Hospital B
	Incidence ¹	3.5		
	Case-fatality	na ²		

¹ incidence per 100 000 children 0-59 months of age

² Not available

Estimated annual burden of childhood Hib disease, *Country (date)*.

District	Hib cases			Hib deaths		
	meningitis	pneumonia	total	meningitis	pneumonia	total
District X						
Meningitis incidence rate method	8	41	49	2	10	12
Under –5 mortality rate method	na	na	na	na	na	na
District Y						
Meningitis incidence rate method	40	200	240	10	20	30
Under –5 mortality rate method	na	na	na	na	na	na
National						
Meningitis incidence rate method	500	3000	3500	150	300	450
Under –5 mortality rate method	800	4000	4800	250	400	650

* Compare these estimates of incidence and disease burden to the estimates from other countries using data from national surveillance, Hib disease burden rapid assessment tool results and population-based surveillance.

Summary of findings

The meningitis incidence rate method (Worksheet 2) estimates that in *country* there are *xx* cases and *yy* deaths each year as a result of invasive Hib disease in young children.

The under-5 mortality rate method (Worksheet 3) estimates there are *xx* cases and *yy* deaths each year.

That these two methods provide a range on what the true estimate of disease is thought to be.

Explain potential limitations of this assessment with special reference to the following:

- case recognition, access to hospitals, use of antibiotics prior to hospital admission, use of lumbar puncture upon admission, laboratory capacity to culture *Haemophilus influenzae*, quality of record keeping in the paediatric ward and laboratory, etc.
- variation among populations in the country.

Recommendations

In light of these findings, the following recommendations might be considered:

- Discuss with Intracountry Coordinating Committee (ICC) results of above, as background for decision to introduce, or not to introduce, Hib vaccine.
- Develop a more complete estimate of Hib meningitis morbidity and mortality through local investigators, for example, at a teaching hospital, and others, as appropriate. Encourage formation of Hib disease working group.
- Enhance capacity of at least two laboratories in *country* to culture and identify Hib in CSF.

Annex 5:

Forms

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Form A: Criteria for guiding the selection of a region for the accurate assessment of Hib meningitis incidence using local data

Population criteria	
1.	More than 250 000 people in the region.
2.	The majority of children in the region (>90%) utilize one (or two) regional hospital(s). (Children with Hib meningitis who do not live in the region but are diagnosed in the regional hospital should not be included in the calculation of the incidence rate. Children who live in the surveillance region and who are hospitalized with Hib meningitis in another region should be included in the incidence rate for the surveillance region.)
3.	Children with meningitis are attended to in the health care system; they do not generally die at home.
4.	There is low use (<10%) of the new Hib vaccine in the private sector in the region.

Hospital criteria	
1.	Paediatric services exist to treat children with bacterial meningitis.
2.	Not more than 40% of children pretreated with antibiotics before arriving at hospital.
3.	All suspected meningitis cases should undergo (be offered) lumbar puncture.
4.	All cerebrospinal fluid (CSF) should be promptly submitted to the laboratory for cell count, biochemistry, direct exam and culture.

Laboratory criteria	
1.	CSF should be transported to lab, examined and plated onto media as soon as possible after being obtained.
2.	Primary cultures of CSF specimen should be done on chocolate agar (supplemented with V factor preferable) or supplemented blood agar (for example, polyvitex or isovitalex). Human blood should not be used.
3.	Incubation should occur at 35-37°C in a 5-10% CO ₂ environment (by candle jar or CO ₂ incubator).
4.	Suspicious colonies must be subcultured onto a nutritionally deficient agar (for example, tryptic soy agar or Columbia agar) with X, V and XV disks or strips placed. <i>H. influenzae</i> will only grow in presence of both X and V factors. ^{1,2}
5.	Quality control checks of the media used should be routinely performed to confirm the ability of the batch to support the growth of <i>H. influenzae</i> .

¹ *H. influenzae* isolates should be serotyped to confirm that they are type b (Hib). Latex kits will detect Hib but they will not identify other capsular serotypes.

² Short-term storage of Hib isolates should be done on chocolate agar slants. Long-term storage should be done by freezing the isolates at -70° C.

Form B: A checklist of important questions and data to be obtained during the assessment

(Data that will be used directly in the Worksheets is indicated in italics)

National ministry of health and other sources

Sources of Information: national ministry of health officials (EPI manager, national disease surveillance managers, ARI programme director, national laboratory manager), consultants, literature review, published statistics (see section IV for suggested sources) and vaccine manufacturers/distributors.

Introduction: We will be using a Worksheet to estimate the burden of severe disease (i.e. meningitis and pneumonia) caused by *Haemophilus influenzae* type b (Hib) in your country. By answering the following questions, you will help us quickly arrive at these estimates. These figures will help the MOH decide if vaccination against Hib is warranted in your country.

Thank you.

General population demographics (national) and other data

Questions/data elements	
1.	What is the total population of the country? <i>(Worksheet 1, Step 3)</i>
2.	What is the population of children less than 5 years of age? <i>(Worksheet 2, Step 0)</i>
3.	How many children are born each year in the country (birth cohort)? <i>(Worksheet 3, step 0)</i>
4.	How many children survive to their first birthday in the country?
5.	What is the neonatal mortality rate in the country (# of children who die before they reach one month of age per 1000 live births)? <i>(Worksheet 3, step 1A)</i>
6.	What is the infant mortality rate in the country (# of children who die before their first birthday per 1000 live births)?
7.	What is the under-5 mortality rate in the country (# of children who die before 5 years of age per 1000 live births)? <i>(Worksheet 3, step 1A)</i>
8.	Which regions of the country have higher infant and under-5 mortality rates?
9.	Which regions of the country have lower infant and under-5 mortality rates?
10.	Are there any important regional differences in vaccine coverage? If yes, Which regions have generally lower coverage? Do any regions have exceptionally higher coverage?

Hib vaccine

Questions/data elements	
1.	Has Hib vaccine ever been used in the EPI programme (for example, sometimes countries obtain one-time donations of Hib vaccine and apply them widely)? If so, when? For how long? How many doses were delivered? In which age groups and what regions?
2.	Is Hib vaccine available in the private sector? If yes, in which regions? How much does it cost? In these regions, what percentage of children receive Hib vaccine through the private sector?

Disease surveillance

Questions/data elements	
1.	<p>Does the MOH conduct national, regional, or sentinel surveillance for meningitis?</p> <p>If so, please provide the following:</p> <ul style="list-style-type: none"> · A copy of the reporting forms used for meningitis surveillance. · Examples of recent reports summarizing the meningitis surveillance data. If these do not include data from the last calendar year, please provide a summary of recent surveillance data. · Is laboratory confirmation required for all cases? · Is zero-reporting practised? · Is the outcome of each case (alive/dead/unknown) recorded? · Is a line-listing of reported cases available for recent years? If so, please provide a copy.
2.	<p>Is a special population-based surveillance study of Hib disease being conducted in your country?</p> <p>If so, where?</p>
3.	<p>Does the MOH conduct surveillance for acute lower respiratory infections (ALRI)?</p> <p>If so, please provide a summary of these data for the last several years.</p>
4.	<p>Are blood specimens taken from meningitis cases typically processed at a national or regional laboratory?</p>
5.	<p>Are CSF specimens taken from meningitis cases typically processed at a national or regional laboratory?</p>
6.	<p>Please provide copies of any reports, publications or studies from your country which focus on Hib meningitis, bacterial meningitis or pneumonia in children.</p>

Selection of region for retrospective meningitis incidence calculations

Questions/data elements	
1.	<p>Which regions of the country fulfil most of the criteria outlined in Form A (regions suitable for calculation of a Hib meningitis incidence rate)?</p>

Optional: Data for economic impact calculations (some countries may want to have this information)

Questions/data elements	
1.	On average in your country, how much does it cost to hospitalize a child for one day?
2.	What is the average length of hospitalization for a child with bacterial meningitis?
3.	What is the average length of hospitalization for a child with bacterial pneumonia?

Regional/local ministry of health offices

Sources of information: regional health officials (EPI manager, communicable disease surveillance officer, communicable disease control manager).

Introduction: We will be using a Worksheet to estimate the burden of severe disease (i.e. meningitis and pneumonia) caused by *Haemophilus influenzae* type b (Hib) in your region and the entire country. By answering the following questions, you will help us quickly arrive at these estimates. These figures will help the MOH decide if vaccination against Hib is warranted in your country.

Thank you.

Regional population characteristics

Questions/data elements	
1.	What is the total population of the region? <i>(Worksheet 1, step 3)</i>
2.	What is the population of children less than 5 years of age in the region? <i>(Worksheet 1, step 4A)</i>
3.	How many children are born each year in the region (birth cohort)?
4.	What is the neonatal mortality rate in the region (# of children who die before they reach one month of age per 1000 live births)? <i>(Worksheet 3, step 1A)</i>
5.	What is the infant mortality rate in the region (# of children who die before their first birthday per 1000 live births)?
6.	What is the under-5 mortality rate in the region (# of children who die before 5 years of age per 1000 live births)?

Health services

Questions/data elements	
1.	Please list all hospitals in the region that treat paediatric patients with meningitis (i.e. public hospitals, private hospitals and military hospitals).
2.	Are children with very severe illnesses (e.g. patients with bacterial meningitis) likely to be referred to hospitals outside of the region?
3.	Do any of the hospitals listed above in (1) serve as a referral centre for children who live outside the region?
4.	Are there any important (subregional) differences in vaccine coverage? If yes, Which areas within the region have generally lower coverage? Do any areas within the region have exceptionally higher coverage?

Hib vaccine

Questions/data elements	
1.	Has Hib vaccine ever been used in the EPI programme (e.g. sometimes countries obtain one-time donations of Hib vaccine and apply them widely)? If so, when? For how long? How many doses were delivered? In which age groups and what regions?
2.	Is Hib vaccine available in the private sector? If yes, in which regions? How much does it cost? In these regions, what percentage of children receive Hib vaccine through the private sector?

Disease surveillance

Questions/data elements	
1.	<p>Does the MOH conduct national, regional or sentinel surveillance for meningitis?</p> <p>If so, please provide the following:</p> <ul style="list-style-type: none"> · A copy of the reporting forms used for meningitis surveillance and indicate the frequency (24h, weekly, monthly) of reporting. · Examples of recent MOH reports or publications summarizing the meningitis surveillance data from this region. If these do not include data from the last calendar year, please provide a summary of recent surveillance data. · Is laboratory confirmation required for all cases? · Is zero-reporting practiced? · Is the outcome (alive/dead/unknown) recorded?
2.	<p>Is a special population-based surveillance study of Hib disease being conducted in your region?</p> <p>If so, where?</p>
3.	<p>Does the MOH conduct surveillance for acute lower respiratory infections (ALRI)?</p> <p>If so, please provide a summary of these data for the last several years.</p>
4.	<p>Are blood specimens taken from meningitis cases typically processed at a national or regional laboratory?</p>
5.	<p>Are CSF specimens taken from meningitis cases typically processed at a national or regional laboratory?</p>
6.	<p>Please provide copies of any reports, publications or studies from your region which focus on Hib meningitis, bacterial meningitis or pneumonia in children.</p>

Hospital visit – paediatric service

Sources of information: chief of paediatric infectious disease service, chief of paediatrics, hospital director, hospital information manager, medical records chief.

Introduction: We will be using a Worksheet to estimate the burden of severe disease (i.e. meningitis and pneumonia) caused by *Haemophilus influenzae* type b (Hib) in your country. By answering the following questions, you will help us quickly arrive at these estimates. These figures will help the MOH decide if vaccination against Hib is warranted in your country.

Thank you.

Meningitis

Questions/data elements	
1.	Is Hib vaccine available in the private sector? If yes, what percentage of children receive Hib vaccine through the private sector?
2.	What percentage of children presenting with suspected meningitis receive antibiotics before arriving at this hospital?
3.	In this region, what percentage of children with suspected meningitis are seen at this hospital? If children in the region are not all seen at this hospital, what other hospitals would they go to?
4.	In your hospital, do you see children with meningitis who reside outside of this region? If yes, what percentage of admissions reside outside the region?
5.	In this region, what percentage of children with suspected meningitis die at home before reaching the hospital?
6.	In this hospital, what percentage of children with suspected meningitis undergo lumbar puncture for CSF specimens? <i>(Worksheet 1, step 3A)</i> If less than 100%, what are the reasons for not performing a lumbar puncture?
7.	How long does it take for a CSF specimen to reach the laboratory after it is taken?
8.	Who transports CSF specimens to the laboratory?
9.	What percentage of children with suspected meningitis have blood specimens taken?
10.	What percentage of children with Hib meningitis die? <i>(Worksheet 2, step 2A; Worksheet 3, step 4A)</i>
11.	What percentage of children with Hib meningitis have severe neurologic sequelae (e.g. deafness, hemiparesis, mental retardation)?
12.	In your opinion, what are the leading causes of meningitis in children in this hospital?
13.	Does your hospital see cases of neonatal meningitis? If yes, what percentage of your meningitis cases are neonates (children less than one month of age)?
14.	Are log books available that record admission and discharge diagnoses, demographic information and discharge status for each patient admitted to the ward?

Optional: data for economic impact calculations (some countries may want to have this information)

Questions/data elements	
1.	What antibiotics do you use to treat clinical meningitis in this hospital?
2.	How many days on average does a child with Hib meningitis receive intravenous antibiotics?
3.	How are children with severe neurologic sequelae, such as mental retardation, cared for in the region/country?
4.	What is the average length of stay in your hospital for a child with Hib meningitis?
5.	How much does one day in the hospital cost for a child hospitalized in your institution (including costs of antibiotics)?
6.	What is the average length of stay in your hospital for a child with bacterial pneumonia?
7.	What antibiotics do you use to treat bacterial pneumonia in your hospital?

Meningitis count from clinical records (from paediatrician and review of meningitis roster and/or paediatric logbook; Form C provides a sheet that assists in making a line listing of meningitis cases)

Questions/data elements	
1.	Dates of review (at least one year of surveillance is needed, more recent years are preferable – e.g. from January 1999 to present).
2.	Total number of suspected bacterial meningitis cases in children <5 years of age (with or without lab confirmation).
3.	Number of suspected bacterial meningitis cases in children <5 years of age which are purulent*. <i>(Worksheet 1, 1A – will need to review tally sheet and compare with microbiology data)</i>
4.	Number of meningitis cases in children <5 years of age in which a bacterial pathogen was identified (by culture, latex, gram stain or polymerase chain reaction (PCR) methods). Please list numbers of each bacteria isolated and record CSF laboratory results if available. The tally sheet in Form C can be used to record cases. <i>(Worksheet 1, 1B – will need to review tally sheet and compare with microbiology data)</i>
5.	Number of meningitis cases in children <5 years of age in which Hib was identified (by culture, latex, gram stain or PCR methods). Please list numbers of each bacteria isolated and record CSF laboratory results if available. The tally sheet in Form C can be used to record cases. <i>(Worksheet 1, 1C – will need to review tally sheet and compare with microbiology data)</i>
6.	Number of these Hib meningitis cases that died.
7.	Hib meningitis case-fatality rate (#6 / #5). <i>(Worksheet 2, step 2A; Worksheet 3, step 4A)</i>
8.	Number of these Hib meningitis cases that had severe neurologic sequelae (e.g. deafness, hemiparesis, mental retardation).

* An accepted working definition for purulent meningitis is finding cerebrospinal fluid that is:

- a. turbid or cloudy, or
- b. ≥ 100 white blood cells, or
- c. 10-99 white blood cells AND glucose < 40 mg/dl AND protein > 100 mg/dl

Pneumonia questions (from review of meningitis roster and/or paediatric logbook)

Questions/data elements	
1.	What are the leading causes of bacterial pneumonia in children in this hospital?
2.	What percentage of children with suspected bacterial pneumonia die?
3.	What percentage of children admitted with pneumonia have blood cultures done on admission?
4.	What are the number of bacterial pneumonia cases in children <5 years old (if difficult to calculate, an estimate is acceptable).

Hospital visit – Microbiology service

Sources of information: chief of microbiology laboratory, chief of clinical chemistry laboratory.

Introduction: We will be using a Worksheet to estimate the burden of severe disease (i.e. meningitis and pneumonia) caused by *Haemophilus influenzae* type b (Hib) in your country. By answering the following questions, you will help us quickly arrive at these estimates. These figures will help the MOH decide if vaccination against Hib is warranted in your country.

Thank you.

General

Questions/data elements	
1.	Are cerebrospinal fluid specimens processed in the hospital lab? If no, are they are processed in an outside lab?
2.	How long does it take, generally, between the collection of the specimen and delivery to the laboratory ?
3.	Does the lab process CSF specimens 24 hours a day, 7 days a week?
4.	What procedures are conducted on the CSF: physical description, cell count, glucose, protein, culturing, typing?
5.	Are log books available that record the results of these procedures?
6.	What percentage of CSF undergoes culture? If less than 100%, what are the criteria for culturing CSF?

Laboratory methods

Questions/data elements	
1.	What types of agar is used for the primary CSF culture?
2.	What type of blood is used to prepare the agar plates?
3.	Is chocolate agar used in your lab? If so, how is it made?
4.	Is either blood or chocolate agar supplemented with anything? If so, what is used as supplement?
5.	Are culture plates incubated? If so, describe apparatus used, temperature, atmosphere and length of incubation.
6.	How do you determine if a colony growing on the primary plate is <i>Haemophilus influenzae</i> ?
7.	Is a control strain of <i>Haemophilus influenzae</i> used in your laboratory? Is every batch of chocolate agar tested to ensure that it will support the growth of the control strain of <i>Haemophilus influenzae</i> ?
8.	Do you save <i>Haemophilus influenzae</i> isolates cultured from CSF? If yes, how do you save them?
9.	Do you send your <i>Haemophilus influenzae</i> isolates to a reference laboratory for confirmation and further testing?
10.	Does your laboratory participate in a proficiency testing scheme for <i>Haemophilus influenzae</i> ? If yes, give details.

CSF specimens (Form C provides a sheet that assists in making a line listing of meningitis cases)

Questions/data elements	
1.	Dates of review (at least one year of surveillance is needed, more recent years is preferable – e.g. from January 1999 to present).
2.	Number of CSF specimens processed in children <5 years of age (if available).
3.	Number of purulent* meningitis specimens in children <5 years of age. <i>(Worksheet 1, 1A – will need to review tally sheet and compare with clinical data)</i>
4.	Number of purulent* meningitis specimens in children <5 years of age in which a bacterial pathogen was identified (by culture, latex, gram stain or PCR methods – please list numbers of each bacteria isolated). <i>(Worksheet 1, 1B – will need to review tally sheet and compare with clinical data)</i>
5.	Number of purulent meningitis specimens in children <5 years of age in which Hib was identified. (Please list as much information about these patients on the tally sheet in Form C). <i>(Worksheet 1, 1C – will need to review tally sheet and compare with clinical data)</i>
6.	Number of CSF specimens in which Hib was isolated but that did not meet the definition of purulent. <i>(Worksheet 1, step 1H)</i>

* An accepted working definition for purulent meningitis is finding cerebrospinal fluid that is:

- a. turbid or cloudy OR
- b. ≥ 100 white blood cells OR
- c. 10-99 white blood cells AND glucose < 40 mg/dl AND protein > 100 mg/dl

Form C: Sample form for collecting information on cases of Hib meningitis

Facility: _____ Time period (dd.mm.yy - dd.mm.yy): _____

	Demographics				Source of case & record number (check all sources where case found)				
	Admission date (dd.mm.yy)	Name	Sex (m / f)	Age (yy.mm)	Region of residence	MOH surveillance	Pediatric ward admission book	CSF log book	Hospital records
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									

Form C: Sample form for collecting information on cases of Hib meningitis (continued)

Facility: _____ Time period (dd.mm.yy - dd.mm.yy): _____

Admission date (dd.mm.yy)	Name	Lumbar puncture	CSF results (check all that apply and note result)						Outcomes	
			Appearance	WBC count	Protein	Glucose	Culture results (NG-no growth)	Latex agglutination results	Discharge diagnosis	Discharge: alive/dead
1										
2										
3										
4										
5										
6										
7										
8										
9										
10										

An accepted working definition for purulent meningitis is finding cerebrospinal fluid that is:

- a) turbid or cloudy, or
- b) ≥ 100 white blood cells, or
- c) 10-99 white blood cells AND glucose < 40 mg/dl AND protein > 100 mg/dl

Annex 6:

Worksheets

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Copies of these MS Excel worksheets may be obtained from the Department of Vaccines and Biologicals or on the Internet at www.who.int/vaccines-documents/Excel/www625.xls

[Click here for copies of the MS Excel worksheets](#) 

Worksheet 1:
Retrospective estimate of Hib meningitis incidence
(enter data in light grey cells
calculated data in dark grey cells)

		Data input
Step 1: Number of Hib meningitis cases diagnosed from CSF		
1A	Number of purulent* CSF specimens in children < 5 years <i>If this information is not available, put "0" in cell</i> <i>Note that only children residing in defined region of interest should be included.</i> <i>if possible, do not count neonatal cases (newborns 0-1 month of age)</i> <i>*Purulent defined as the following:</i> <i>a. turbid or cloudy OR</i> <i>b. > 100 white blood cells OR</i> <i>c. 10-99 wbc AND glucose < 40 mg/dl AND protein > 100 mg/dl</i>	
1B	Number of purulent meningitis cases from 1A in which a bacterial pathogen was identified <i>(Bacteria can be identified by positive culture, latex agglutination test or gram stain)</i>	
1C	Number of purulent meningitis cases from 1A in which Hib was identified <i>(Hib can be identified by positive culture, latex agglutination test or gram stain showing gram negative coccobacilli)</i>	
1D	Percentage of purulent meningitis cases with a bacterial source identified due to Hib $(1C / 1B)$	
1E	Number of purulent meningitis cases from 1A in which NO bacterial pathogen was identified $(1A - 1B)$	
1F	Number of purulent meningitis cases in which no bacterial pathogen was identified which were likely due to Hib $(1D \times 1E)$	
1G	Total number of cases of Hib meningitis with purulent CSF in region in children < 5 years of age during time period of surveillance $(1C + 1F)$	
1H	Hib isolated from nonpurulent CSF <i>(cases in which Hib was found but CSF did not meet purulent definition listed above)</i>	
1I	Number of months of surveillance used to obtain values in 1A - 1C	
1J	Number of years of surveillance	
1K	Annual number cases of Hib meningitis in region in children < 5 years of age $(1G + 1H / 1J)$	
Step 2: Estimating Hib meningitis cases among children who did not get lumbar puncture <i>If 100% of children with suspected meningitis get lumbar puncture, put 100 into 2A and proceed to step 4.</i>		
2A	Percentage of children with clinical meningitis who get lumbar puncture	
2B	The annual number of cases of Hib meningitis that were missed in children who did not get lumbar puncture $(1K / (2A/100) - 1K)$	

Step 3: Estimating the number of children < 5 years of age in region of surveillance <i>If known, the annual population of children < 5 years of age in the region of surveillance can be entered directly into 3A below. If unknown, proceed through steps 3B1 - 3B5 below.</i>		
3A	Annual population of children < 5 years of age in region of surveillance	
3B1	Total annual population of country	
3B2	Annual population of children < 5 years of age in country	
3B3	Percentage of national population < 5 years of age ($3B2/3B1$)	
3B4	Total annual population in region of surveillance	
3B5	Annual population of children < 5 years of age in region of surveillance ($3B3 \times 3B4$)	
Step 4: Calculation of the incidence rate of Hib meningitis in children < 5 years of age in the region of surveillance		
4A	Total number of Hib meningitis cases in children during period of surveillance ($1K + 2B$)	
4B	Annual incidence rate of Hib meningitis per 100 000 children < 5 years of age in region of surveillance ($4A/(3A \text{ or } 3B5) \times 100\,000$)	

Worksheet 2:
Estimating the local burden of Hib disease
Hib meningitis incidence rate method
(enter data in light grey cells
calculated data in dark grey cells)

		Local data
Step 0: Population data		
	Number of children < 5 years old in country	
Step 1: Hib meningitis cases		
1A	Incidence of Hib meningitis <i>(number of cases per 100 000 children < 5 years old)</i>	
1B	Annual number of Hib meningitis cases <i>(1B = 1A / 100 000 x number of children < 5 years old)</i>	
Step 2: Hib meningitis deaths		
2A	Hib meningitis case-fatality rate <i>(enter as a percent)</i>	
2B	Annual number of Hib meningitis deaths in children < 5 years old <i>(1B x 2A)</i>	
Step 3: Estimate the number of Hib pneumonia cases		
3A	Ratio pneumonia:meningitis cases	
3B	Annual number of Hib pneumonia cases <i>(1B x 3A)</i>	
Step 4: Estimate the number of Hib pneumonia deaths		
4A	Hib pneumonia case-fatality rate <i>(enter as a percent)</i>	
4B	Annual number of Hib pneumonia deaths <i>(3B x 4A)</i>	
Step 5: Summary Hib meningitis and pneumonia		
5A	cases <i>(1B + 3B)</i>	
5B	deaths <i>(2B + 4B)</i>	

Worksheet 3:
Estimating local burden of Hib disease
Under-5 mortality rate method
(enter data in light grey cells
calculated data in dark grey cells)

		Local data
Step 0: Population data		
	Annual number of live births in country	
Step 1: Hib pneumonia deaths		
1A	Under-5 mortality rate <i>(number of deaths per 1000 live births)</i>	
1B	Neonatal mortality rate <i>(number of deaths per 1000 live births)</i>	
1C	<i>U5MR - Neonatal mortality rate</i>	
1D	Percentage of childhood deaths from ARI <i>(enter as a percent)</i>	
1E	Annual number of deaths from ARI in children < 5 years old <i>(excluding neonates) (live births x 1C / 1 000 x 1D)</i>	
1F	Percentage of ARI deaths due to Hib <i>(enter as a percent)</i>	
1G	Annual number of Hib pneumonia deaths <i>(1E x 1F)</i>	
Step 2: Hib pneumonia cases		
2A	Hib pneumonia case-fatality rate <i>(enter as a percent)</i>	
2B	Annual number of Hib pneumonia cases <i>(1G / 2A)</i>	
Step 3: Hib meningitis cases		
3A	Ratio pneumonia:meningitis cases	
3B	Annual number of Hib meningitis cases <i>(2B / 3A)</i>	
Step 4: Hib meningitis deaths		
4A	Hib meningitis case-fatality rate <i>(enter as a percent)</i>	
4B	Annual number of Hib meningitis deaths in children < 5 years old <i>(3B x 4A)</i>	
Step 5: Summary Annual Hib meningitis and pneumonia		
5A	cases <i>(2B + 3B)</i>	
5B	deaths <i>(1G + 4B)</i>	