

PD-ABU-130  
11173

**Lombok *Haemophilus influenzae* type B (Hib)  
Vaccine Project  
Six-Month Report  
January – June 2000**

**Submitted to:**

**United States Agency for International Development  
under the USAID-supported ARIVAC Project  
Cooperative Agreement #HRN-A-00-95-00025**

**Submitted by:**

**PATH  
(Program for Appropriate Technology in Health)  
4 Nickerson Street  
Seattle, WA 98109**

**July 2000**

-1-

**Lombok *Haemophilus influenzae* type B (Hib) Vaccine Project  
Six-Month Report  
January – June 2000**

**Summary**

Primary activities of the Lombok Hib Vaccine Project during this period were the expansion of the study area on the island and improvement of case finding and referral. These changes were motivated by the need to accelerate accumulation of study endpoint cases in order to finish the study within a reasonable timeframe. The study population was expanded by 38 percent in May and June. In addition, several new staff were hired at both the Ministry of Health (MOH) and PATH offices to improve community case finding, hospital referral, and supervision.

**Slower than expected case accumulation**

A Hib Study Team management meeting, held in February, reviewed the 1999 data and determined that the end-point target of 630 cases of radiological pneumonia was not being achieved at the anticipated rate. The primary reasons are a lower than expected rate verifying radiologically-confirmed pneumonia among severe pneumonia cases, as well as a series of "leakage points" in the steps of case collection, from vaccination to successful X ray in the hospital. Specifically, there was a "leakage" in each of the steps of: on-time vaccination, case identification, referral to health center, referral to hospital, and readable X ray taken at the hospital. The leakage of each of these steps was small—typically 5-10 percent—but in the aggregate, the lost cases represent a significant loss of potential endpoint cases.

The management team decided on a two-part approach to increase the case-accumulation rate: expansion of the study area by approximately 33 percent (the actual expansion turned out to be a 38 percent increase), and steps to reduce the case leakage by 33 percent. The team estimates that these changes will result in study completion in August 2002 instead of late 2003, as based on the 1999 data.

**Study expansion**



Twenty-three additional villages were selected, based on the likelihood that each will contribute a substantial number of cases to the study. Wherever possible, the villages selected are associated with an already-operational Hib study health center. Training sessions were held in April and May for participants in the networks of community surveillance and health center staff. These sessions covered study activities, case identification, referral, incentives, immunization, and reporting/recording mechanisms. The new villages began referring patients in May, and immunizing with study vaccines in June.

**Reduction of case-accumulation leakage**

As a first step to improving case identification and referral, project staff conducted a community-based survey among family members to determine their understanding of the Hib vaccine study

and to characterize their attitudes and practices towards infant illness. The survey revealed a lack of understanding of the study process and incentives, as well as negative feelings toward hospitalization. To overcome these misunderstandings and hospital issues, the project hired five new staff to work among the mothers in the villages and the hospitals. In coordination with health center staff, these community motivators identify problem areas in which to work. The motivators spend time with village social leaders and mothers to explain the study, remind them of the importance of identifying fast breathing and convulsion cases among their children, and the importance of taking them to the health center. They also spend time in the hospital wards, talking with the mothers and providing information and patient advocacy to improve the families' impressions of the hospital visits. Initial reports indicate that these community- and hospital-based activities are successful in improving case referral and hospital satisfaction. In May, the first month these efforts were operational, the hospital referral rate increased to 92 percent from a study average of 86 percent.

### **Vaccination**

Vaccination activities continued successfully. The study expansion will result in approximately 4,100 doses delivered to children each month—an increase from the pre-expansion rate of 3,000 doses per month. Cold chain capacity has been adjusted to handle the additional vaccines. As of May 2000—the most recent available figures—48,071 doses of study vaccine have been delivered to 18,763 children (those receiving one or more dose(s)).



### **Outcome data**

Attached are two graphs showing death and pneumonia rates among the children enrolled in the study that are being monitored as part of the study surveillance system. Seasonal rates of pneumonia may be due to a number of factors, including the rainy season and RSV cycles. In general, the graphs show gradual improvements in case identification and referral rates.

### **Radiology**

Members of the Hib Study Steering Committee are active participants in a series of World Health Organization (WHO) meetings to establish simplified standards for interpretation of X rays for field studies. Hib study X rays will be read in accordance with WHO criteria, with additional information collected as appropriate. Study team efforts are ongoing to match the X ray criteria and reading procedures with WHO recommendations. Poor X ray quality continues to be a small—but noticeable—problem. Several efforts to improve quality are being implemented, including better coordination of study-provided X ray supplies, quality review meetings, and strengthened oversight by pediatricians.

### **Adverse events during this period**

Dr. Gessner performed an analysis of all hospital admissions and child deaths among the study population, as well as the relationship of the event to the time of their vaccination. His analysis showed that the rate of admissions and deaths among children within one week of vaccination was similar to the rate one to two weeks after vaccination. This indicates a low likelihood of adverse events being related to vaccination. A meeting of the Data and Safety Monitoring Board

(DSMB) was held in May to discuss this analysis. Three sets of adverse-events reporting forms—describing deaths within a few days of vaccination—were submitted to the DSMB during the period. The DSMB is currently reviewing these cases.

### **Cost-impact study**

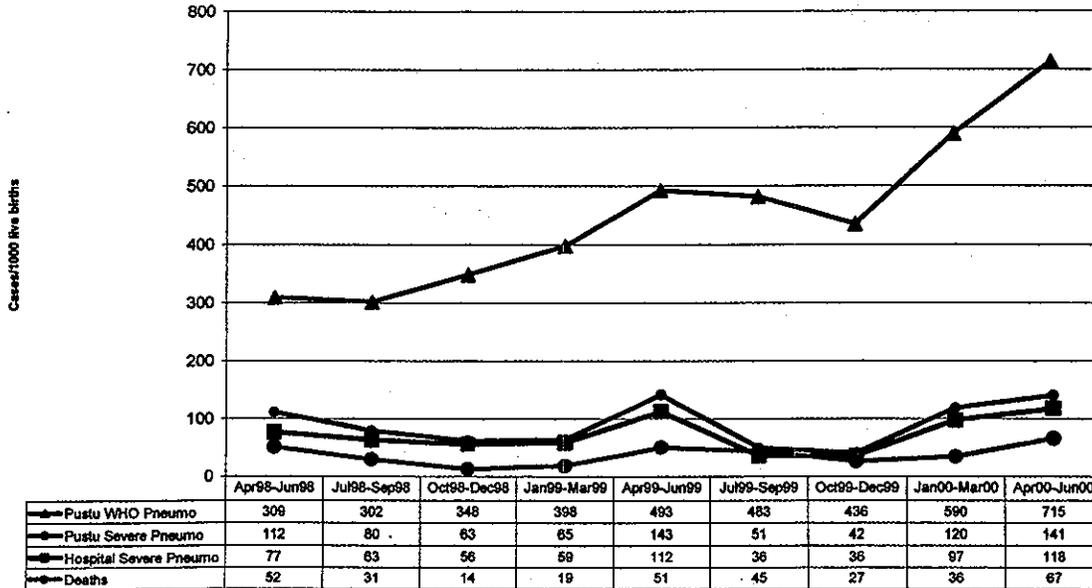
Dr. Jack Molyneaux and two Indonesian health economists have been hired as consultants to conduct a cost analysis of the incidence and treatment of Hib disease compared to the costs of providing Hib immunization in Lombok. Dr. Molyneaux has made two visits to the site, and is currently preparing a protocol and schedule of the cost study. In June, he and other members of the study team and Steering Committee attended a WHO-sponsored meeting of participants in pneumococcal vaccine trials, as well as vaccine manufacturers, to discuss ways to perform vaccine cost-analysis studies. The title of the meeting was "First Meeting of the Working Group for Economic Evaluation of Pneumococcal and Hib Vaccines." The Lombok study was considered an excellent site to conduct such an analysis.

### **Budget issues**

PATH's project costs to date have been co-funded predominantly by USAID under the Acute Respiratory Infections Vaccine Project, and minimally by the National Vaccine Program and the Bill and Melinda Gates Children's Vaccine Program (CVP) through PATH. The Association of Preventive Medicine's (AMP's) costs have been supported by Pasteur Mérieux Connaught, the Mérieux Foundation, and the Government of France. Total costs of the study, to date, have been approximately \$2,300,000 for PATH's costs—including AMP's contribution to the local costs. (These figures do not include AMP's management costs.) Now, however, with the expansion of the study population by 38 percent, and the extension of the study until mid-2002, considerably more funding is required to complete the work. The projection is for PATH's costs—including AMP's participation in supporting the local costs—to be approximately \$5,500,000.

Although USAID/Washington has agreed to grant a no-cost extension to PATH through the end of the study term, no additional funding from this source is available. USAID/Jakarta has committed to supporting the cost of the cost-effectiveness component of the study—probably in the range of \$50,000. AMP may still be able to increase their support of the local costs of the study, but their donor has not yet made a commitment. Meanwhile, CVP has agreed to considerably increase its allocation of funds to this project through the end of 2002, although the exact contribution by each party is yet to be determined.

**LOMBOK Hib PROJECT**  
**Pneumonia Risk**  
 children 2-23 months of age  
 (April 98 - June 00)



**LOMBOK Hib PROJECT**  
**Mortality rates**  
 children 2-23 months of age  
 (April 98 - June 00)

