Policy Study of Factors Influencing the Adoption of New and Underutilized Vaccines in Developing Countries

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Executive summary

i. Introduction

A number of effective vaccines are available but not yet included in National Immunization Programmes (NIPs), while still more are near to licensure. Two vaccines which the World Health Organisation (WHO) has recommended for inclusion in the Expanded Programme on Immunization, but which have not been introduced in many of the countries in greatest need, are Hepatitis B vaccine (HBV) and yellow fever (YF) vaccine. The high effectiveness of HBV is now established, but the introduction of universal HBV globally has been relatively slow. Although 34 African countries are at-risk for yellow fever, only 17 include YF vaccine in their NIPs, and in 1994 and 1995 six African countries reported outbreaks of the disease. *Haemophilus influenzae* type b (Hib) vaccine is highly effective against a major cause of meningitis and pneumonia in children under five. Since pneumonia is estimated to underlie 18% of deaths in developing countries, the inclusion of affordable Hib vaccines in NIPs is a major challenge.

This study examines the factors which facilitate and constrain the adoption of new and underutilized vaccines in developing countries. It looks specifically at HBV, YF and Hib vaccines. Taking a multi-disciplinary policy analysis approach, methods used included a thorough review of available materials including four recent studies commissioned by the Children's Vaccine Initiative (CVI), extensive interviews with key informants, visits to Geneva, Washington and London, and attendance at key meetings. Data collection took place between June and November 1998. Although interviewees were asked to comment on their experience in, and perceptions of, decision-making in developing countries, the investigators did not visit any developing countries, and in this stage of the study were not able to elicit the views directly from the country level.

ii. Contextual factors affecting vaccine introduction

Four contextual factors were noted. First, the *rapid expansion of immunization* in the 1980's services and the important role of international organisations (particularly WHO and UNICEF) in promoting and funding such services was highlighted. This led to some degree of dependence on donors, although this differed from region to region. Second, *changes in funding*, have affected NIPs, as funds for routine immunization programmes declined after 1990. Non-polio funds for WHO's Global Programme on Vaccines (GPV) only increased from US$ 15.5 million in 1994 to US$ 18 million in 1997. During the same period, funds specified for polio eradication increased from US$ 4 to US$ 43 million. The recurrent costs associated with the procurement of vaccines, and particularly newer vaccines, has become a key concern of donors and governments leading to the development of a tiered system of funding in the early 1990s. This tiering system has affected vaccine policy. The other two contextual factors which have influenced the uptake of vaccines have been *decentralization*, where health services are increasingly implemented under district rather than central control; and the *adverse economic environment*, which has affected the willingness and ability of countries to commit to, and sustain payment for new vaccines.

iii. Influences on the decision-making process

We identified several factors which affect the decision-making process. *The long timeframe* for the introduction of any vaccine has to be juxtaposed against frequent changes of people decision-making positions making continuity difficult. *New vaccines can affect existing NIPs*. There is evidence to suggest concern exists over difficulties with multiple formulations and combinations in procurement and implementation. The *importance of data, including cost-effectiveness studies, and the way data are used*, was acknowledged, and its absence or inaccessibility to decision-makers was sometimes seen as a cause of delay in introducing vaccines. However, many other unquantifiable factors affected acceptance. *Vaccine efficacy and effectiveness* were a high priority

for decision-making by the international community, while the effect of *price and perceived affordability*, relative to GNP were most associated with vaccine adoption at the national level, and therefore likely of greater concern to national policy-makers.

iv. The central role of actors in decision-making

The study suggested three explanations for perceived caution in introducing new vaccines into national immunization programmes. First, there is no clear consensus or leadership at the international level in the promotion of new vaccines. Where once country policy makers would have expected leadership from WHO and UNICEF, both organisations are at junctures in their histories which constrain such leadership. Second, there are a number of other organisational actors interested to take the initiative on vaccines. Interviewees pointed to the real efforts being made to negotiate the potential for links between public and private sectors, and to search for mechanisms of collaboration. The World Bank, for example, has shown considerable interest in promoting new vaccines; organisations such as Rockefeller, PATH and the new Melinda and Bill Gates' Foundation Children's Vaccine Programme are strong supporters of new vaccines. While there is general support for the attempts being made to find mechanisms for collaborating with industry, difficulties in reaching agreements and continuing concerns about public-private governance make this a slow process. And finally, the study drew attention to the absence of voices from developing countries themselves, suggesting that insufficient space has been allowed for national views to be expressed, with relatively little understanding of, or priority given to policy-making environments.

v. Concluding discussion

The findings from this study, and others, suggest that a number of different explanations are helpful in considering the process of adoption of "new" vaccines (specifically HBV and Hib) and existing vaccines (yellow fever). While decisions to introduce new vaccines are not merely economic, procurement financing and economic constraints have played a major part in determining whether new vaccines are introduced into NIPs. There is no doubt that HBV was slow to be accepted until the price declined in the early 1990s. Six themes were highlighted:

Adoption of new vaccines is part of a political process and takes time

One of the concerns driving this study was that countries have been slow to adopt new vaccines, and that existing vaccines such as yellow fever have been neglected. While the latter is certainly an issue, it is less clear that progress has been tardy in relation to new vaccines. Measles vaccine was licensed in the USA in 1963, yet it took over 20 years to get it introduced in Asia. Measles coverage continues to be low in West and Central Africa where mortality is highest. Thus the apparent slow introduction of HBV is not surprising.

However, there does appear to have been a major failure with yellow fever. The study provided many different insights into why this has been a lower priority vaccine, ranging from a historical drop in scientific interest in arboviruses (influenced by the hiatus in funding after Rockefeller shifted priorities); the 'hidden' nature of disease – described as an 'out of sight, out of mind' disease; no clear case definition; poor laboratory facilities; many unanswered technical questions over strategies; its relative lower priority in the face of major, highly visible problems such as meningococcal epidemics; and no clear advocates at country, regional or international level (although this may now be changing).

There is confusion over vaccine priorities and policies

There has been no clear and consistent international message to say that new vaccines are a high priority. The vision and consensus, mediated and catalysed through international champions such as James Grant, Albert Sabin and Jonas Salk which characterised immunization programmes in

the 1970s and 1980s, has dissipated. However, the study found that attributing any confusion over policy or lack of consensus on the value of new vaccines to 'lack of political will' is simplistic. The decision-making process is itself complex and there is genuine uncertainty about what policy approaches are best in the long term. Interviewees were divided, and the international community often takes polarised positions, on whether it is best to assist countries through vertical disease programmes or through building up health infrastructures.

There are real dilemmas facing both donors and national policymakers in choosing between many multiple and competing policy and funding priorities. However, donors themselves are involved in the process of decision-making at the international level, and it is the multi and bi-lateral agencies which put different and competing potential programmes on the policy agenda.

Policies on vaccines are supply-driven not demand-sensitive

Although the study did not look at decision processes at the country level, from interviews and other studies it seemed that in the past vaccine policy has largely been decided by international and regional experts and donors, and that few countries have a clearly enunciated policy on the introduction of new vaccines into NIPs. This is partly a reflection of the way international agencies behave. Many emphasize international actions in promoting new vaccine introduction, expressed as 'filling the vaccine pipeline', identifying local 'salesmen' or advocates to make the case.

However, as past willingness to pay for vaccines has declined, the point of decision has shifted to the country level. Increased responsibilities for funding, decision-making and integrating new vaccines are now being put on countries. If countries are expected to take greater responsibility for the introduction of new vaccines, then international agencies will have to be more demand-sensitive. Country demand and willingness to commit resources, not solely international pressure on the supply side, will be essential features in any expansion of NIPs.

Varying perceptions of 'affordability' lead to inconsistent policy positions

Findings suggest that 'affordability' is a contested concept. For many countries' public health systems, new vaccines remain relatively expensive. Even with decreased costs, prices are a much higher percentage of GNP in developing than in developed countries, and costs of research and development, production and regulation are increasing. New vaccine prices are unlikely to fall to levels comparable to the original six EPI vaccines.

The perception of 'affordability' is central here. For developed countries, even expensive vaccines may be good value, if seen as an investment in the future. The significant level of resources necessary to complete polio eradication is worthwhile to the industrialized world because of the huge benefits it will bring. For developing countries, however, especially low-income countries, the costs are considerable (even where many of the resources are external), and new vaccines may have less importance than addressing other pressing disease problems. In developing countries, the fixed costs of EPI are about $14, while the original 6 vaccines cost approximately $1 in total. Additional antigens cost between $0.5-3 per dose. Even allowing for price tiering for poorest countries (so that they pay only 20% of the market cost of vaccines) new vaccines continue to make up a much larger percentage of per capita GDP than in industrialised countries.

Technical problems have been underplayed

In the enthusiasm to make new vaccines available to larger numbers of people, it appears that some difficult technical questions have been overlooked. For those concerned with actual delivery of programmes at the country level, this may be a strong factor in waiting to see how policy and

strategy develops in relation to new vaccines before their inclusion in NIPs, which on the whole, have already solved problems of dosage, timing, cold chains and so on for the original 6 antigens.

Advocacy is more influential than any other factor in facilitating change
An effective advocate or champion can be more influential in facilitating vaccine adoption than any other factor, particularly at the country level. Numerous interviewees noted the absence of global vaccine advocates. The importance of advocacy within an agency for building up support in a programme of work, and in having one or two individuals within the agency with sufficient authority and leeway to persuade others - whether groups or individuals - was mentioned by many.

vi. Recommendations

1. Advocacy is essential, and long term strategies should be devised to explore ways of facilitating change. The report identified a number of strategies, such as identifying champions or advocates at the international, regional and national level; gaining the interest and support of top politicians such as ministers of health, heads of state or key figures in the business community; working with parliamentary committees to get legislation on immunization among others.

2. Top consideration must be given to the format of information as well as the position of spokespersons and messengers conveying data on new vaccines.

3. Particular effort needs to be made at the international level to resolve differences and inconsistencies in vaccine policies, with clearly demarcated functions for different organisations. Leadership and coherence needs to be revived.

4. International organisations should be assisting countries to set priorities for immunization, develop plans of action, and plan for ways of raising funds, geared to individual country circumstances, political and health systems.

5. The introduction of new vaccines should be used to reinforce and support existing infrastructures. Statements on new vaccines being made available only for those countries with high coverage rates should be re-visited on grounds of equity.

6. Attention needs to be given to generation of funds for new vaccines, without prejudicing the polio eradication campaign’s completion.

7. International organisations should improve their understanding of decision-making processes at the country level, and strengthen mechanisms for getting nationals’ voices heard.

8. Attention should be paid to translating international policy advice into practice, by devising practical guidelines and helping managers incorporate new vaccines.

9. The positive experiences from PAHO and WPRO in the promotion of new vaccines should be shared across regions.

10. In order to facilitate debates and reach consensus on national and regional priorities, clear strategies are needed to ensure eradication programmes do not hinder the introduction of new vaccines in low income countries.

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List of Abbreviations

AFRO	African Regional Office (WHO)
BCG	Bacille Calmette-Guérin (TB) Vaccine
BoD	Burden of Disease
CDC	Centre for Disease Control (USA)
CE	Cost-effectiveness
CVP	Bill and Melinda Gate's Children's Vaccine Programme
CRS	Congenital Rubella Syndrome
CVI	Children's Vaccine Initiative
DFID	Department for International Development (UK)
DTP(3)	Diphtheria/Tetanus/Pertussis Vaccine (3 doses)
EMRO	Eastern Mediterranean Regional Office (WHO)
EPI	Expanded Programme on Immunization
EU	European Union
GAG	Global Advisory Group
GPV	Global Programme for Vaccines and Immunizations
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Vaccine
Hib	*Haemophilus influenzae type B*
HIV	Human Immunodeficiency Virus
IVI	International Vaccine Institute
MMR	Measles/Mumps/Rubella Vaccine
MOH	Ministry of Health
NGO	Non-Governmental Organisation
NIP	National Immunization Programme
OPV(3)	Oral Polio Vaccine (3 doses)
PAHO	Pan-American Health Organisation (WHO)
PHC	Primary Health Care
SAGE	Scientific Advisory Group of Experts
SEARO	South-East Asia Regional Office (WHO)
TFSA	Task Force on Situation Analysis of Vaccine Supply (CVI)
UCI	Universal Childhood Immunization
UNDP	United Nations Development Programme
UNICEF	United Nations Children Fund
USAID	United States Agency for International Development
VII	Vaccine Independence Initiative
WB	World Bank
WHA	World Health Assembly
WHO	World Health Organisation
WPRO	Western Pacific Regional Office (WHO)
YF	Yellow Fever

1. Introduction

Background

Immunization programmes have spearheaded the development of public health worldwide. Through immunization, over 3 million deaths are averted each year, and the eradication of poliomyelitis is drawing near. Health professionals around the world have been trained to use a range of simple tools to plan, manage and monitor their programmes, and resources have been mobilized for the benefits of vaccines to reach most of the world's population. Lessons learned about simplifying immunization schedules, providing protection as early in life as possible, establishing and disseminating clear practice standards and guidelines, developing inter-agency coordinating committees, and monitoring indicators of both process and impact have benefited industrialized countries as well as developing countries (Cutts and Olivé, 1999). Efforts to ensure the supply and quality of vaccines are underway. A range of new vaccines are under development against major pathogens.

Introduction of additional vaccines

A number of effective vaccines are available but not yet included in National Immunization Programmes (NIPs), while still more are near to licensure. Two vaccines have for several years been recommended for inclusion in WHO's Expanded Programme on Immunization (EPI) but are still not widely used in may of the countries where disease burden is highest: Hepatitis B vaccine (HBV) and yellow fever vaccine. Hepatitis B results in more than one million deaths every year worldwide (WHO/UNICEF,1996). The high effectiveness of the vaccine has been demonstrated by dramatic reductions in the carrier rate in immunized cohorts of children (Fortuin et al, 1993). In Taiwan, 10 years after implementation of a mass vaccination programme, a fall in the annual incidence of hepatocellular carcinoma in children aged 10-14 years has already been documented (Chang et al, 1993). However, introduction of universal HB vaccination globally has been determined more by the economic status of the country than by its disease burden. Although 34 African countries are at-risk for yellow fever, only 17 include yellow fever vaccine in their NIP, and the Gambia is the only country to have achieved high coverage and impact on disease (GPV, 1998a). In 1994 and 1995, outbreaks of yellow fever were reported in six African countries (Robertson et al, 1996).

Haemophilus influenzae type b (Hib) vaccine is a highly effective vaccine against a major pathogen. In The Gambia, it had an efficacy of over 90% against invasive Hib disease, and significantly reduced the incidence of radiologically-defined pneumonia by 21% (95% CI, 4.6-34.9%) (Mulholland et al, 1997). Since pneumonia is estimated to underlie 18% of deaths in developing countries, the identification of mechanisms to make Hib vaccine affordable to children in the poorest countries is a major challenge for the international health community.

Rubella vaccine has been used for almost 30 years in industrialized countries. A review completed for the World Health Organization (WHO) in 1995 showed that seven developing countries have documented rubella outbreaks with congenital rubella syndrome (CRS) incidence rates as high as those in industrialized countries pre-vaccination (Cutts et al, 1997). All seven countries now have national rubella vaccination policies. Although 28% of developing countries already include rubella vaccine in their national immunization programmes, many countries need further data urgently to determine the relative priority to give to control of CRS (Robertson et al, 1997). Its integration into the EPI has not yet been recommended by WHO.

Lower respiratory infections and diarrhoeal diseases were among the top four causes of death worldwide in 1990 (WHO/UNICEF, 1996), and vaccines that are under development against these diseases have immense potential to improve health status. Some new vaccines will be licensed for the existing EPI target groups, e.g. rotavirus vaccine, conjugate pneumococcal and meningococcal vaccines; some will be targeted at adolescents, e.g. herpes virus vaccines, HIV vaccines, and others will be indicated for persons of all ages, e.g. dengue, malaria (CVI, 1998d).

The Policy Study

This report represents the findings of the first phase of a project commissioned by the Children's Vaccine Initiative (CVI) and United States Agency for International Development (USAID). It brings together existing information on the key factors that influence adoption of new and underutilized vaccines in developing countries, with a focus on the international community's understanding of the adoption process. Only limited data was collected from developing countries. A second phase is planned to access countries' experiences in vaccine introduction.

Collaborating Institutions

The first phase of the policy study was conducted by the following collaborating institutions: London School of Hygiene and Tropical Medicine (LSHTM), University of California at San Francisco (UCSF), WHO/GPV, CVI, and USAID. Felicity Cutts, M.D. (LSHTM) served as project co-ordinator. Gill Walt, Ph.D. (LSHTM) provided policy consultation and Alan Brooks, R. N., MSc. served as research associate. Judith Justice, Ph.D., MPH (UCSF) collaborated with the LSHTM on all aspects of the study. Interviews were conducted by Judith Justice and Alan Brooks, and Felicity Cutts provided information from meetings in Africa.

The collaborating team was selected to bring together a multi-disciplinary approach to study the process of adoption of new vaccines. The members of the team represented medical, nursing, epidemiological, public health, policy analysis, and social science expertise.

Time Frame

Collection of data began in June 1998 and was completed in November 1998. This report of the first phase of the project includes the review of the available written resources (both published and unpublished), and an analysis of new data collected from key individuals, funding organizations, and manufacturers, combined with a summary of the findings of other studies conducted by WHO/GPV and CVI.

Methods

Review of Available Materials

A review of the published literature was made to identify relevant references and issues. Medline and the Bath Information Services databases were searched from 1981 to 1998. In addition to published materials, an in-depth review was made of unpublished sources, including studies, meeting reports, technical reports, annual publications, and budgets from the World Health Organization/Global Programme on Vaccines (WHO/GPV) and the CVI. Relevant reports and information from other international and bilateral donor organizations, individuals, and vaccine manufacturers were reviewed and included in the analysis.

Information was also available from other studies conducted by WHO/GPV and CVI, which included the following:

- a case study of the experience of four countries with the adoption of the *Haemophilus influenzae* type B (Hib) conjugate vaccine. Conducted in Uruguay, Chile, Qatar, and Kuwait,

the first countries in Latin America and the Middle East to adopt Hib, and therefore called "early adopting" countries, the study was carried out by a collaborative team from CVI, GPV/WHO/HQ, PAHO, EMRO, and CDC. The report, *Introduction of Hib Conjugate Vaccines: Experience in Four 'Early Adopting' Countries* (1998), was written by Jay Wenger, EPI/WHO and CVI.

- A three-country comparison of the influence that the private sector may have on public sector decisions to incorporate new vaccines into national immunization programmes. This study was conducted by Yvette Madrid, consultant to GPV/WHO, who made country visits to Morocco, Thailand, and Zimbabwe in 1998.

- A quantitative analysis of data useful for assessing vaccine priorities and policies, as well as the epidemiological and cost predictors of new vaccine use, is being completed by Dr. Mark Miller of CVI.

- A report of the experience of vaccine manufacturers in distributing new vaccines, prepared by Louis Freidel, a retired official from the marketing division of a vaccine company.

Interviews

This phase of the policy study used primarily qualitative methods for collection of information. Formal and informal interviews were conducted with individuals identified (using snowball techniques) as playing a role in the international vaccine field. These included global leaders in the field, scientists, academics, policy analysts, medical officers, representatives of multi-national and bi-national donor organizations, non-governmental organizations (NGO's), and vaccine manufacturers. Information was collected from past and potential future funding agencies for vaccines. These agencies include multi-national and bi-national donors, international and regional banks (World Bank, Asian Development Bank), and NGO's. Eighty people were interviewed (Appendix 1) to document their past experience and perceptions of current factors that influence the adoption of new vaccines and predictions for the future. Special attention was given to regional experience in order to identify variation related to geographic location and regional differences. However, few people from SEARO or EMRO were interviewed, and as in previous studies of the sustainability of Universe Childhood Immunization (UCI) and eradication programmes, the Eastern Mediterranean region has unfortunately been under-represented.

Guidelines were prepared for these interviews which were conducted by phone and in-person. The guidelines included questions designed to elicit information on the interviewee's background and experience in the field of vaccines, perception of factors that influenced the adoption of new vaccines or served as barriers to the introduction of new vaccines. Questions addressed the interviewee's perception of the decision-making process for adopting new vaccines; individuals and organizations at the international and country level who were influential in the decision-making process; the type of data that was available and influenced decision-making at the international and country level; the importance of cost as a factor; views on funding mechanisms to facilitate the adoption of new vaccines; and, the importance of regional variations.

Visits

When possible, field visits were made to meet key informants and collect other forms of data. Two researchers visited WHO in Geneva to interview relevant staff of GPV, EPI, and CVI. A visit to Washington, D.C. was made to meet with representatives from the World Bank, PAHO, USAID, National Institutes of Health, and other individuals. Officials in other regions were contacted in person, by phone or electronically. Collaborators attended the Scientific Advisory Group of Experts on Vaccines (SAGE) in June 1998, the CVI Consultative Group Meeting in

November 1998, and the World Bank Working Group "Informal Consultations on Improved Mechanisms for Global Immunization Effort" in London on 5-6 October and in Geneva on 7 November 1998.

Framework for the study

The study used a policy analysis approach (Walt and Gilson 1994) looking at contextual factors which affect policy formulation and implementation, processes of decision-making and actors involved. The next three sections of the report reflect this approach. However, although useful conceptually, it is clear that context, process and actors cannot be clearly separated and that each is strongly inter-related. Section 2 looks at some of the contextual factors affecting vaccine introduction. Section 3 addresses key factors such as the utilization of data and information to inform decision-making processes, and section 4 explores the central role of actors in the process of identifying, formulating, developing and implementing policy. The final sections, 5 and 6, draw conclusions and make some recommendations.

2. Contextual factors affecting vaccine introduction

Rapid expansion of immunization services and donor-dependence

In 1974, when the EPI began, only 4% of infants in developing countries received diphtheria-tetanus-pertussis (DTP) and polio vaccines, and a heat-stable measles vaccine had not yet been developed. Donor and government investment in primary health care and the EPI helped to develop health services infrastructure in developing countries, with extensive support from WHO for training managers at all levels. In 1983 the goal of 'Universal Childhood Immunization by 1990' (UCI) was proposed by UNICEF and later supported by WHO. Investment in EPI increased exponentially, most funds being channelled through UNICEF. The greatest achievement of UCI was reported to be raising coverage of infants to levels of 80% in a few years. This contributed to a significant reduction of mortality and morbidity in children. By combining simple and effective technologies in service delivery with the advocacy necessary to mobilize interest and resources, coverage increased at rates never before seen.

Many national health systems and donor organizations were essential partners in UCI, but the special leadership role played by UNICEF and its late Executive Director, James Grant, is widely recognised. A review of factors affecting the sustainability of immunization programmes in the African, South-east Asian and Western Pacific regions was conducted for UNICEF in 1995 (UNICEF, 1996). It found that at the country level, UNICEF was viewed as a 'can do' agency that was able to use its influence and resources effectively to energize people and programmes. Support was leveraged to bring immunization services up to scale. UNICEF usually began acceleration activities with a visit from James Grant which built support for immunization at the highest political level. Often, heads of state or their designees agreed to take an active interest in service delivery and UNICEF helped to provide information on progress and needs to those in power (UNICEF, 1996).

Improved immunization helped to show that ministries of health could provide services, and that low coverage pointed to the need for management and administrative changes. It contributed to the improvement of systems necessary for PHC in many countries. Immunization was described by some as the 'locomotive that pulled the train'.

In middle income countries and many of the low income countries, immunization has remained a high priority and the infrastructure that was developed has been built on to tackle control of major diseases. The period since 1990 however, has challenged the proponents of immunization to develop an approach to guarantee sustained achievement in low income countries. Coverage in some countries has stabilized or declined, particularly in the poorest countries and those affected by conflict. John (1998) and Murugusampillay (1994) and some interviewees considered that the process through which UCI had been implemented in low income countries had failed to develop mechanisms to sustain achievements. EPI decisions were simplified and removed from the country's health sector, leading to a lack of ownership of vaccine programmes in the public sector medical community. Countries were not given the expertise to make strong decisions which could lead to the introduction of additional vaccines (e.g. ability to conduct their own cost-benefit measurements). During 1980's, programmes relied on extensive external resource support and were felt to be donor driven in low income countries. External funds covered training costs, per diems for outreach, supervision and social mobilization. These activities were difficult to maintain, because local ownership and the funding that would follow strong commitment by governments did not always materialize.

In most of Africa and Asia, evaluation of UCI was mainly based upon output (coverage) instead of impact (decreases in disease), with relatively limited investment in surveillance systems. This has led to a situation in many countries in which it is difficult to obtain data on disease burden (as discussed more fully in section 3) which would help to promote the introduction of new vaccines.

The situation in the Americas has been somewhat different. This region changed from a goal of achieving a certain coverage level to disease control/eradication goals earlier than other regions (de Quadros, 1994). This had certain advantages (PAHO, 1995). Firstly there was no artificial "cut-off date" by which a goal could be declared as achieved. Thus, commitment to immunization continued without interruption beyond 1990. Second, emphasis was put on surveillance at a relatively early stage, to monitor progress towards polio eradication in particular. The skills, interest and laboratory support needed for surveillance were built on in the 1990s to obtain data needed for introduction of new vaccines, as discussed later. Lastly, strong mechanisms for social mobilization and for donor co-ordination were developed through the immunization/polio eradication programmes. These have been well sustained and used to advantage to implement recent decisions regarding introduction of additional vaccines. Thus, the infrastructure and processes of negotiation with different actors (see section 4) that were developed in the Americas seem to be more conducive to taking on new vaccines in this region than in poorer, more heterogeneous and donor-dependent regions**.**

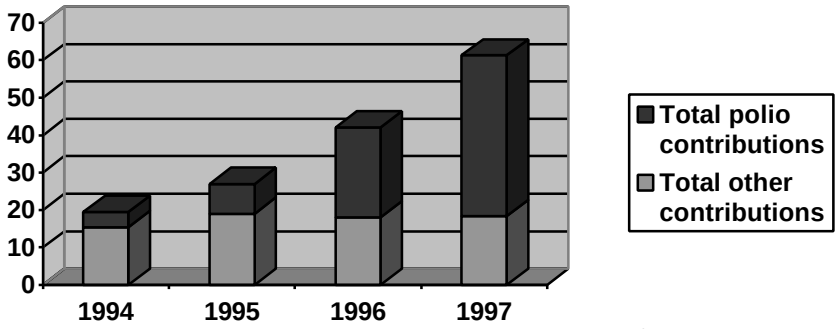
Changes in funding

Funds for routine immunization programmes declined after 1990, and the policies of donor agencies changed, as discussed more fully in section 4. Although the polio eradication programme has led to renewed investment in the last 5 years, funds are more closely targeted to the specific polio goals and few donors are willing to continue providing funds to sustain the physical and human resource infrastructure for the routine immunization programme. A recent review of the EPI in the African region noted that the infrastructure (especially the cold chain) for routine programmes in many countries has deteriorated, and a guaranteed source of long-term funding to rectify this has yet to be identified (GPV, 1998c).

Funding for GPV initiatives, aside from that specified by donors for polio eradication, saw little growth in the 1990's (See Figure 1). Non-polio funds increased from US $15.5 million in 1994

to US $18.1 million in 1997. During the same period, funds specified for polio eradication increased from US $4 million to US $43 million. Four donors are largely responsible for the increase in polio funds: Australia targeting the Western Pacific Region, Denmark targeting India, and the USA and Rotary International for use in most WHO regions. The figures for polio do not include increased national contributions or UNICEF vaccine purchases. They also do not reflect effects of the eradication initiative on the EPI system (GPV, 1998b).

Figure 1: Evolution of donor support for polio and all other GPV initiatives, 1994-97 (US$ Millions)



Reproduced from GPV, 1998b

One of the most significant changes since 1990 has been the increasing tendency to shift the financial burden of vaccine procurement from donors to countries. The reluctance of donors to continue funding the same consumable items indefinitely has been further aggravated by increasing vaccine prices, new initiatives which require more vaccines to control target diseases, and the planned introduction of new and improved vaccines. Incorporation of HBV into immunization programmes in just those countries with a carrier rate of greater than 8% will cost an estimated US$100 million per year at current prices (Batson et al, 1994).

New vaccines are an order of magnitude more expensive than the traditional EPI vaccines. Vaccine costs may fall when the number of manufacturers increases, particularly if developing country manufacturers can be involved. Muraskin (1995) describes the efforts made to involve Korean business in the manufacture of HBV in order to bring down the costs from the $30 per dose being charged by Merck, to $1 per dose.

On the procurement side, there are two potentially conflicting strategies to try to bring down the costs of vaccines. UNICEF initially used its large-scale procurement activities to negotiate low costs. By the early 1990s, UNICEF absorbed 40-60% of manufacturers' total output of a particular vaccine (Institute of Medicine 1997;85). This approach is still used effectively by Dr. Ciro de Quadros of PAHO, who uses economies of scale, purchasing for the region, to negotiate lower prices. PAHO's approach assumes that all countries should pay the lowest price possible for vaccines. The PAHO revolving fund allows countries greater flexibility and buying power when purchasing vaccines, and has been used for large scale procurement of Hib and MMR which are not typically offered through UNICEF.

UNICEF's policy on procurement of vaccines for developing countries has changed markedly over the last decade. In 1991 UNICEF began the Vaccine Independence Initiative (VII), modelled on PAHO's revolving vaccine fund (DeRoeck, 1998). VII was intended to encourage middle income countries to increase funding of their own vaccine needs, thereby freeing donor

support for countries in greater need and new vaccines. VII has proved itself moderately successful, encouraging 14 middle income countries to finance more or all of their vaccine needs and facilitating new vaccine introduction in a limited number (e.g. The Philippines). It appears to have facilitated donor support for new vaccine introduction in only one case; Australia and New Zealand supporting hepatitis B vaccine for the Pacific Island nations (DeRoeck, 1998).

In November 1994, UNICEF announced a new "vaccine support strategy" that made procurement decisions targeted towards countries in greatest need. This followed the "UNICEF/Mercer study of the vaccine industry" which concluded that by subsidising richer developing countries in their purchase of vaccines, UNICEF was inadvertently antagonizing the commercial sector, whose co-operation was needed, and diverting its funds away from those most in need (Muraskin 1998; 230).

When the goals of the CVI were formulated it was recognised that little progress could be made in the provision of new vaccines unless the existing problems in vaccine supply were overcome. The Task Force on Situation Analysis of Vaccine Supply of the CVI was established to address this problem.

The first step taken was the development of a logical framework to analyse global vaccine needs and potential supply systems (Batson et al, 1994). Two key factors, population size and national wealth, were selected. A graph was developed using population size and GNP per capita as axes. This graph was further divided into nine segments on the basis of World Bank income groupings and estimates of population size needed to support vaccine production. The position of an individual country on the grid gives an indication of the extent to which it might need external support, the type of support it requires, and the degree to which it can cater for its own vaccine supply needs through procurement or production of vaccines. Countries were placed in bands according to the degree of need of donor funds and the type of assistance needed.

The development of this tiering system was rapidly applied and has been highly influential in changing policy with regard to funding vaccines. Donors and international agencies frequently allocate funding according to a country's classification. International vaccine manufacturers also began to tier vaccine prices according to country band. Band A and B country prices typically reflect production and overhead costs, and potentially a small profit. Band C country prices reflect a greater amount of research and development costs as well as the expected profit margin. Band D and E country costs reflect full retail value of vaccines.

Table 1: Illustrates expected self-financing levels according to country bands, and the percentage of countries achieving target levels.

Self-Financing Targets for 1999			
Band	**Target Financial Contribution to Vaccine Needs**	**Countries Reaching Target (1990)**	**Countries Reaching Target (1995)**
A	10-25%	2%	25%
B	80-100%	40%	70%
C	100%	80%	90%
D & E	100%	100%	100%

Adapted from GPV, 1997a

The procurement of vaccine has become a key focus of donors and governments (Shin and Shahi, 1994). This will help to ensure one critical input, but does not address the equally critical availability of operational funds for reaching children. This trend was identified with mixed impressions by interviewees. Vaccines are widely perceived as a free or cheap commodity in the developing world after years of receiving the antigens through donor funds. The European Union (EU) and France in Africa, as well as PAHO in Latin America have pushed countries to begin inserting budget lines for vaccines. EU and French donor funds are channeled through the line in the national budgets. The funds are then tapered off, leaving the country to find funds to meet its now established budgetary needs. Many countries are struggling to pay an increasing share of the costs of the original EPI antigens and infrastructure. The costs of new vaccines become an additional challenge. Some have suggested banding slows new vaccine introduction and gives donors an excuse not to fund vaccines for countries that are not classified as 'in the greatest need'. Industry representatives, however, were extremely supportive of the banding system. They felt that in order for tiered prices to be viable, the market would need to be artificially segmented as is accomplished by the banding strategy. Industry representatives interviewed expressed concern about the approach used by PAHO as it allowed low and middle income countries to pay equal prices for vaccines.

Decentralization

Immunization programmes in developing countries have traditionally been organized under a centralised system, predominantly through the public sector. Thus Ministries of Health (MOH) were responsible both for setting policies and norms, and for managing programmes. Donor support was given via the MOH which controlled the budget for immunization. MOH personnel, often with technical assistance from donors, trained and supervised peripheral health workers at district and health centre levels. With ubiquitous health reforms however, this structure is changing in many countries, although there is great diversity between countries and regions.

Two of the health sector reforms promoted by international agencies are decentralization of implementation of health services and the promotion of the private sector. Countries vary in the degree to which either of these reforms have been implemented. Where the decentralisation process is most advanced, health services are under local government control, budgets are managed at district level, and the role of the MOH focuses on policy-making and advice. Donors may supply funds to, and work directly with, health managers at district level. The growth in the private sector and its role in immunization is less easy to measure, although in the poorest countries it is still relatively small. Many governments are struggling to adapt to the changing roles demanded by health reforms, further weakening decision-making capacity at national level.

Adverse international economic environment

The broader context in which immunization programmes operate has also changed markedly over the last decade. Global forces that affect health policies and systems in developing countries include the dominance of the market approach, and the increase in poverty and inequality within and between countries as well as violent civil conflict within and between nations. Healthcare systems worldwide absorb an increasingly large share of resources. In 1990, public and private expenditure on formal health services reached 8% of total world product. Industrialized countries spent almost 90% of this amount, with average per capita expenditure on health care about $1500. In contrast, developing countries spent an average of only $41 per capita, and many of the poorest countries spent less than $5 (Lafond, 1994). In the past 15 years, structural adjustment policies for economic reform, promoted by international banks, have cut government health care budgets by a third to a half in most sub-Saharan African countries (Evans, 1995). Sizeable sums of public money continue to be spent on tertiary level hospitals at the expense of cost-effective interventions delivered at primary level. Access to basic health services remains low in many

rural and dispersed communities. At the same time official development assistance has declined to below $0.3 per capita, its lowest level in real terms for 25 years (Nelson et al, 1996). The involvement of the private sector (including for-profit services, missions and non-governmental agencies) in health care is increasing in all countries, raising challenges not only for equitable access to care but for co-ordination, standardisation and quality control of interventions.

Recent global economic instability impacts the willingness and ability of developing countries to commit to and sustain payment for new vaccines. The economies of South Asia have been slow to recover from the impact of the 1997 financial crisis. Indonesia is in the midst of its worst economic downturn in 30 years. The financial strength of Thailand and South Korea have been shaken. Multinational wars in Western and Central Africa destabilize and impact the limited financial strength of the entire region. Latin America's instability and Brazil's recent currency devaluation reflect the global economic turmoil. In the Middle East, oil prices remain at their lowest levels in decades, leading to multibillion dollar deficits in economies accustomed to substantial surpluses.

Without a confident economic outlook and stable currencies, countries may be hesitant to commit long term resources to vaccine introduction. The perceived affordability of new vaccines diminishes. Country willingness to assume further debt through World Bank loans to pay for vaccines in the face of an unstable economic picture remains to be seen. Madrid (1998b) noted the vulnerability of Thailand to economic troubles, suggesting that the public sector which introduced hepatitis B vaccine in 1992 is at risk of not being able to meet its health commitments. However, at a CVI Consultation meeting in 1998 Supamit Chunsuttivat said that since HBV was already in the system it would be maintained, but the proposed introduction of Hib had been put on indefinite hold because of the economic situation. Brazil's economy is fluctuating and the recent devaluing of its currency made vaccines purchased through international tender 21% more expensive within a matter of days, as well as diminishing its buying power within PAHO's revolving fund.

3. Key factors in the decision-making process

Timeframe for introduction

It takes at least 6-12 years for a vaccine to proceed through trials to licensure and large-scale production (Levine, 1997). It is an additional 10-15 years or more from licensure in the first country to wide-scale use in NIP's in low and middle income countries (Mahoney, 1998). In total, it is likely to be upwards of 20 years from early clinical trials to wide-scale use of a vaccine in developing countries. At the country level, it often requires at least 4 to 5 years of deliberations from the time the idea is first proposed before a commitment is made to introduce a new vaccine (CVI, 1998d). During this period, there are likely to be many changes in managers and key policy makers at national and sub-national level, making continuity of decision-making difficult.

Hepatitis B vaccine was first licensed in 1981 as a plasma-derived product. A recombinant DNA product produced from yeast was introduced in 1986. Resolution WHA 45.17 of the 1992 World Health Assembly recommended a phased introduction of HBV, with priority given to countries with high carrier rates, followed by universal usage by 1997. As an indication of the time taken to introduction, Zimbabwe expects to introduce HBV in 1998-99, 17-18 years after its earliest licensure, while Thailand required 11 years (Madrid, 1998b, 1998c). Seventeen years after HBV was first licensed, and far longer from the earliest clinical trials, less than half of the world's children receive HBV, and few children in Africa receive the vaccine.

Conjugate Hib vaccine was first licensed in 1988. The earliest introductions of Hib vaccine in Latin America occurred 6 and 8 years later in Uruguay and Chile respectively. In the Middle East, Qatar and Kuwait took 5 and 9 years respectively after first licensure (CVI, 1998a). In 1997, the CVI/WHO-GPV Special Advisory Group of Experts (SAGE) recommended Hib use where there were adequate finances and an established burden of disease. It also encouraged disease burden studies in areas without data. Hib vaccine currently costs between $1.5 to $3 for each of three recommended doses. In 1998, about 16% of countries, primarily in the developed world, were using Hib vaccine in their national immunization programme (Personal communication, Jay Wenger).

Effect on the immunization programme

CVI evaluated four non-industrialised countries that were leaders in their respective regions to introduce Hib vaccines as a routine infant immunization (CVI, 1998a). Standardised questionnaires and site visits to Chile, Uruguay, Kuwait and Qatar and were used to evaluate the introduction of Hib conjugate vaccines. A number of persons in the Ministry of Health, clinical and administrative services were interviewed, but the primary source of information in each country was the NIP manager.

Three of the four countries ran formal introductory or training sessions to familiarise programme personnel with the new vaccines. In one of these, the initial training was noted to be minimal since the vaccine was supplied mixed in liquid form with DTP, and essentially, was handled exactly as DTP by immunization personnel. In three of four countries, education of the public was done primarily through their health-care providers, and no major publicity campaign was performed. None of the countries said they needed any additional cold chain or transportation equipment, or experienced difficulties with introduction in these areas (the report noted that these were relatively high income countries, so this finding may not be generalisable to countries with poorer infrastructure). Similarly, costs of reprinting record-keeping material (immunization cards, ledgers, etc). were uniformly considered minimal. Data on vaccine wastage and coverage were not available at the initial visit. Coverage data collection was been added to EPI coverage surveys. Interest in vaccine wastage is high, and is currently being investigated.

Each of the countries noted that the response to the Hib conjugate programme was positive from public sector providers, and from the public in general. It was suggested that the response of the public in Latin America was enhanced by concern about meningitis in general, presumably as a result of recent meningococcal group B meningitis outbreaks in the area. Impact data from the two countries using Hib vaccine for at least 2 years showed decreases in documented Hib disease by 80% and 95%.

Two issues were raised as substantial problems with introduction. First, 3 of 4 countries noted the price of the vaccine was an issue for continuation of the programme and continued efforts at justification were required to sustain the programme. Secondly, all four countries had substantial difficulties in dealing with multiple formulations and combinations in procurement and implementation of immunization. One country, in changing suppliers as a result of an open tender, decided to switch from monovalent Hib to Hib/DTP combination. However, since they had a large supply of DTP from another manufacturer in stock, which could not be mixed with the Hib, they temporarily suspended Hib immunization until they used the remainder of the DTP. In another country, shifting from liquid to lyophilized formulations necessitated retraining of immunization personnel from one year to the next. A third country has decided to use monovalent Hib as a separate injection specifically to avoid issues of juggling the immunization schedule every time a new tender is made. All respondents noted that a liquid Hib preparation,

preferably with DTP, was the easiest to administer in part due to lack of necessity for reconstitution and avoidance of issues about stability of the reconstituted lyophilized product.

The importance of data

The wording of WHO and UNICEF statements (Appendix 2) has consistently highlighted the importance of the burden of disease and the relative affordability of the vaccine in determining when a country should include new vaccines in the national EPI. In addition, data on the vaccine's characteristics are considered important in WHO's framework for evaluating a vaccine for the EPI (Appendix 3).

Different data may be important at different times and for different groups of decision-makers. At the international level, data on disease burden must show that the disease is of sufficient import to justify investment in vaccine development. Since most work on vaccine development occurs in industrialized countries, data may not be obtained early on from developing countries. Conversely, diseases which are only of public health importance in developing countries may not attract investment from industrialized countries.

Data on vaccine efficacy are clearly needed in order to licence a vaccine. Again, efficacy is usually demonstrated first in trials in industrialized countries. Prior to recommendation for global use, efficacy must be confirmed in tropical countries. Clinical trials of new vaccines in developing countries may precede, or run concurrently with, studies of disease burden. Indeed, vaccine trials may themselves provide the best estimates of the burden of disease, for example the Gambian trial of Hib demonstrated the large proportion of all pneumonias that is caused by this organism.

Once vaccine effectiveness has been established and measures of disease burden obtained, the cost-effectiveness of vaccination can be estimated. As discussed in more detail below, cost-effectiveness data appear to be most important to international decision-makers, while at the country level absolute cost and perceived affordability are more important. Finally, all data must be available and presented in a format that stimulates action by decision-makers.

Disease burden

The meaning of "burden" varies by method of measurement and/or analysis (table 2). The World Bank has used Disability Adjusted Life Years. Dr**.** Mark Miller uses per capita years of life lost (mortality) and disease carriage rates in his quantitative analysis (see below). A representative of a European donor also felt mortality was most convincing. Most interviewees felt any epidemiologically sound approach was sufficient. Comparisons between regions and studies may be more difficult if standard definitions are not used. It remains unclear if one format is of greater benefit to decision-makers at the country level, or how each definition relates to a decision-maker's or peripheral health-worker's perceptions of the disease burden.

Table 2: Definitions of Disease Burden:

Incidence rate
Severity
Mortality rate
Years of life lost
Disability adjusted life years (DALY's)
Quality adjusted life years (QALY'S)
Costs to health services
Costs to patients and families

In the study of early Hib vaccine adopters, all respondents noted that an appreciation of the burden of Hib disease was a key factor in making a decision to adopt the vaccine. In two countries, it was specifically noted that not only the incidence of disease, but also (and possibly more importantly) awareness of the severity of disease, in terms of death and long-term morbidity, was critical to the decision. Reported impact of Hib vaccine in reducing disease in other countries was also important.

The scientific community, manufacturers, and donors (e.g. WHO, USAID) give priority to the availability of the highest quality data on burden of disease and vaccine characteristics. Data were said to be needed of sufficient quality "to convince WHO". WHO and international agencies especially USAID frequently fund or support disease burden studies. At the country level, epidemics, public or government perception of the disease, or media pressure may stimulate interest in establishing the disease burden. In Fiji, paediatricians concerned about the burden of bacterial meningitis established the number of culture-confirmed cases of Hib in the three largest hospitals, without precisely quantifying the disease rate. The data was sufficient to initiate further studies, a trial of Hib, and eventually routine use.

Vaccine manufacturers attempting to increase the market of a vaccine which may have been designed for the developed world are a vital source of funds for data collection. The current initiative through the International Vaccine Institute (IVI) to support multi-centre Hib studies in Asia represents a substantial commitment on the part of 5 manufacturers. Manufacturers also fund more limited studies. Concern was raised by an individual working at the regional level that manufacturers approach countries and get commitments for studies without national level decision-makers fully understanding the implications of the commitment.

In many countries, disease burden data are difficult to obtain and this was described in interviews as a cause of delays in introducing vaccines. This is best reflected by the lack of Hib adoption in Asia. In Africa, although the burden of disease associated with hepatitis B is widely established, cost remains a more important cause of delays. A significant problem for the introduction of yellow fever and rubella vaccines is the extreme difficulty in measuring the burden of disease.

Improving data on burden of disease is one of CVI's current strategic goals (1997b). CVI identifies four problems associated with recognising the disease burden caused by a pathogen:

- Failure to recognise a particular pathogen's contribution to syndrome with multiple aetiologies
- Poor surveillance or lack of studies on the disease burden
- Local norms under-playing the occasional serious consequences of a disease (e.g. measles in industrialised countries)
- Failure to be aware of the true treatment costs entailed in coping with cases of disease (CVI, 1998d)

While data on burden are useful to help set priorities at the international level, country level experience suggests that the quality of data is not the determining factor in its use. Although disease burden data are useful, the *perception* of the problem by key actors was often admitted to be more important than the actual burden of disease. Factors influencing perception of disease included the following:

- *Family or personal experience with a vaccine-preventable disease:* It was only after the child of an official in the Israeli MOH was ill that Hib became a priority leading to introduction. In

Indonesia, HBV introduction was facilitated after the President's golf partner developed liver disease.

- *Knowledge of disease outbreaks:* The resurgence of yellow fever in Africa in the late 1980's led to increased emphasis on the need for vaccination. A series of regional meetings has culminated in the development of an Action Plan for vaccine introduction over the next three years. In Latin America, generalised public concern about meningitis increased due to recent group B meningococcal meningitis outbreaks. This public concern was felt to facilitate Hib introduction in Uruguay and Chile.

- *Coverage of disease in the local media***:** The media played a role in developing interest in Hib vaccine in Latin America as related above. It also played a substantial role in the introduction of HBV in The Philippines. A manufacturer brought the discussion to newspaper, television and radio, raising the anxiety of the public and government officials and eventually forcing the MOH to introduce the vaccine (Dayrit, 1998).

- *Age group affected by disease:* At the global level, children's causes draw great interest. The early perception in UNICEF that hepatitis B was an adult disease delayed and/or provided an excuse to not fund the vaccine. At the country level, interviewees suggested the age affected may have a range of implications. Paediatricians may not see end stage, adult liver disease so may perceive less need to advocate for infant vaccination. Alternatively, some suggested that since adults develop the disease, government officials are *more* willing to introduce HBV. The relative willingness of countries to focus on infant versus adult problems and priorities is greatly impacted by culture.

- *Primary location and risk-group for disease:* Diseases occurring in different geographical regions or perceived as affecting marginalized groups may not be perceived as priorities by decision-makers. YF outbreaks are typically confined to rural settings. Urban decision-makers may be less receptive to or cognizant of the disease's true impact and severity.

- *National scientific and/or medical community's awareness of the disease:* The professional community was widely noted to hold great sway in many countries. Its voice of concern or advocacy through expert advisory groups, formal or informal roles in the government may bring a disease to the attention of decision-makers. Country of training also influences perceptions of health professionals. Doctors in the Middle East were reported to be aware of Hib disease having seen the impact of vaccines during training in the US. Participation in international, scientific meetings was reported to be a frequent conduit for information about important diseases and new vaccines. Industry often funds international conferences and numerous anecdotes described intensive lobbying and product advertising associated with such events.

- *Country capabilities:* Scientific and medical training varies greatly between countries. Those countries with the skilled staff and financial base to support surveillance and diagnostic activities are likely to have a perception of diseases which differs from those countries relying on regional or global estimates to understand their disease burden

- *Neighbouring countries:* The experience of a neighbour introducing a vaccine may raise the disease's profile, bringing it to the attention of EPI staff. The influence may reflect hegemonic interactions between nations (e.g. Australia influencing the South Pacific; South Africa influencing southern Africa). Disease perception may also reflect a change in the "moral

baseline" of the vaccines deemed essential to provide (e.g. it has become unacceptable for NIP's in WPRO countries not to include HBV.)

Vaccine efficacy and effectiveness

At the 1997 SAGE, the necessity of efficacy trials was reiterated, and the usefulness of effectiveness trials was addressed although it was recommended that "introduction should not be delayed unduly to obtain such [effectiveness] data" (GPV, 1997b) – (see paper by Clemens et al 1996, for detailed explanation of these terms). The efficacy and licensing of Hib vaccine was established in developed countries approximately 5 years before landmark field trials in developing countries in the 1990's. A study in The Gambia established efficacy while effectiveness was addressed in Chile (Mulholland, 1997; Lagos, 1996).

Trials are most often supported by international organizations, such as WHO, together with bilateral donors (e.g. USAID, DFID), and industry. Although previously most industrial input was from European manufacturers, American pharmaceutical industries are becoming more interested in the global market with the availability of Hib, rotavirus, and pneumococcal vaccines and, therefore, increasing their contribution to developing country trials. Field trials were widely reported to create demand for new vaccines in the countries where the trials were conducted. It was seen as a moral commitment for the international community to make the vaccine available to the trial country for a period of years if it was found to be effective. Sustainability once the support is withdrawn remains questionable.

Industry also uses trial data for licensing and marketing within countries. Many countries have licensing agencies reviewing vaccine data, with varying degrees of efficiency. Madrid (1998a, 1998b, 1998c) found delays of 3 months to over 2 years associated with licensing vaccines at the country level. However, these delays were inconsequential in terms of the total time required to introduce vaccines in the public sector in developing countries.

In addition to the need for data on vaccine efficacy from high quality field trials, other factors identified as being important included the type of trial, where it was conducted, and what the results demonstrated. For example, the Hib trials conducted in Uruguay and Chile were influential in the adoption of Hib in other Latin American countries. The importance of trials conducted in the Gambia for Hib and currently for pneumococcal vaccines was frequently noted by the interviewees, but information from African countries is needed to confirm this perception. Another trial in South Africa designed to demonstrate the effectiveness of pneumococcal vaccine for lowering the death rate is expected to influence decision-makers.

Cost-effectiveness studies

Most interviewees considered that cost-effectiveness (CE) studies are valuable. CE data have been used to prioritise vaccines at the World Bank in its 1993 report, and more recently in draft policies at the Asian Development Bank. In wealthier, middle income countries, CE data presumably help to convince decision-makers of priorities. These countries have some financial flexibility and ability to invest in health benefits which may only give returns in the long-term.

There is, however, scepticism about the importance of CE data in introducing a new vaccine. Many bilateral donors and countries have been reluctant to give priority to new vaccines, even with strong CE data, in the face of multiple global demands. Many interventions are considered cost-effective while few are acted upon. Hepatitis B and Hib vaccines, and vitamin A supplementation are among the many well-established and widely cost-effective interventions which are not generally used. There are multiple possible causes: lack of immediate or sustainable capital; differences in time frames, paying the costs now, while not seeing the savings

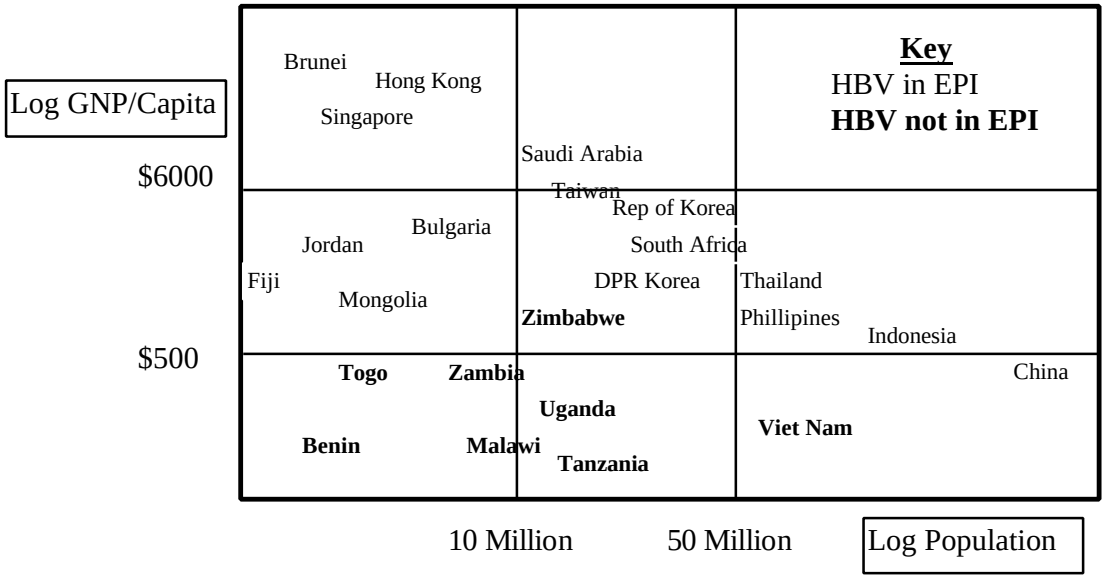
until far down the line; and/or different groups paying the costs now versus seeing the benefits later may also limit adoption. The frequency of investment in non-cost-effective interventions is well recognized; tertiary care still accounts for over half of the health budget in most countries. Changing such spending patterns is extremely difficult.

In countries which are donor-dependent, the decision to adopt a new vaccine is most likely to be influenced by donor agencies. Many of the poorest countries still have less than 50% coverage of the six original EPI vaccines and face structural challenges including developing vaccine delivery infrastructure. A new vaccine may be cost-effective, but not affordable. One estimate suggests India is an extremely cost-effective site for use of Hib vaccine at less than $50 US per DALY saved. The vaccine is not considered affordable because the intervention's net cost per child less than 5 years old is over 1% of per capita GNP (Miller, 1998c). The actual price per dose is a major determinant.

Price and affordability

The status of introduction of hepatitis B, yellow fever and Hib vaccines as of December, 1998 is shown in Appendices 4-6. The studies by Wenger, Miller and others clearly show the importance of the country's income in determining the ability to include new vaccines. Figure 2 shows countries which meet the criteria proposed by WHO for giving priority to HBV introduction (high disease burden and high EPI vaccine coverage), according to their GNP/capita. The GNP appears to be a constraining factor on introduction of the vaccine.

Figure 2. Income and Routine Usage of Hepatitis B Vaccine
Countries with EPI Coverage>70% & HBsAg ≥ 5%



Modified from Kane, 1998

Dr. Mark Miller of CVI is completing a quantitative analysis to assist in defining vaccine policy and priorities. The findings reaffirm that Hepatitis B and Hib are extremely cost-effective interventions. Dr. Miller's analysis identifies three variables predictive of vaccine adoption by NIP's: 1) Vaccine cost relative to per capita GDP; 2) Strength of EPI infrastucture (DTP3 coverage); and 3) Disease burden (per capita years of life lost or disease prevalence).

Table 3 represents preliminary results of the Hepatitis B model, using hepatitis B carrier rates to estimate disease burden. A model encompassing the three variables is 87% predictive of hepatitis B vaccine adoption into NIPs. Vaccine cost as percentage of GDP is most strongly associated with HBV adoption. Hib, YF, and rubella models are pending.

Table 3: Predictors of Hepatitis B Vaccine Uptake into National Immunization Programmes

Variable	Variable target level	Strength of association with HBV adoption
Vaccine cost as % of per capita GDP*	<0.5%	6.5x
EPI infrastructure (DTP3 coverage)**	>80%	3.5x
Disease burden (HBsAg Prevalence)***	≥8%	1.4x

Personal Communication: January, 1999, M.Miller

*****Countries with hep B vaccine cost <0.5% of per capita GDP were 6.5 times more likely to have adopted hepatitis B vaccine.
**Countries with EPI coverage >80% were 3.5 times more likely to have adopted hepatitis B vaccine.
***Countries with HBsAg prevalence =8% were 1.4 times more likely to have adopted hepatitis B vaccine.

The effective use of data

Many interviewees noted that although data exist at the international level, public health decision-makers at regional and country levels may be unaware of the data. Examples were given of international health professionals working in African countries in the late 1980s who were unaware of information about new vaccines such as Hepatitis B and another example of data not being available to WHO regional offices. Posting of GPV/WHO position papers on the internet is a recent attempt to increase the flow of general information on newer vaccines. Country-level data also may not reach the required audience.

When data were presented, this was often reported to be in forms which made it inaccessible and difficult to interpret and use, particularly to the non-scientific community and to decision-makers. Data collection is most frequently done by researchers in academic settings, and the strength of links with public health professionals vary between and within regions. Researchers interviewed for this study identified their own disconnection from decision-makers, confirming that data is frequently intended for consumption by an academic or highly specialised community.

Data is only as good as its use. Data on disease burden was referred to as the "best marketing tool" at the country level by an industry insider. Industry's support of studies reinforces the importance they place on it. Latin America was mentioned by interviewees as a region where strong data on disease burden has facilitated vaccine introduction. Both references assume that the data will be delivered effectively and convincingly to the appropriate decision-makers, whether it is an industry representative or Dr Ciro de Quadros who is presenting the data. The form in which information is presented, and the presence of a respected champion of a vaccine are thus important determinants of how data are used, particularly at country level.

Ultimately, when a vaccine is valued, it receives priority status. Thailand spends approximately 23% of its vaccine budget on rabies vaccine, while HBV and HBV-DTP account for 35% of the budget. Rabies vaccine is perceived as valuable, regardless of the relatively limited associated disease burden, estimated at only 40,000 deaths globally per year. Thailand has an estimated 3,600,000-4,800,000 chronic carriers of hepatitis B (WHO, 1995; Madrid, 1998b).

4. The central role of actors in promoting new vaccines

Decisions about the introduction of additional vaccines are made at many different levels and are influenced by individuals in many different positions. From the 1970s, there was strong international consensus on the need for countries to develop expanded immunization programmes for the six childhood diseases, and to establish infrastructures to sustain such programmes. This consensus was mediated through international organisations such as UNICEF and WHO, through EPI and UCI, expanding to include other agencies later as part of the Task Force on Child Survival. What is clear from country experiences and interviews conducted for this study is that this process of decision-making was strongly driven by the international community (Murugasampillay, 1994, John 1998). Where countries were strongly donor-dependent the decision-making process was extremely weak within countries, with national managers relying on international guidelines and financial support to the extent that programmes were seen to be 'owned' by outsiders. Budget lines for vaccines were not included in planning; data concentrated on outputs and not on impact, so that surveillance systems were not established. It was only in the mid to late 1990s that burden of disease studies began to give national decision-makers data on which to base decisions. Further, the experience of donor dependence, competition between donors at the country level, and top-down or vertical programming has made it much more difficult for nationals in extremely resource-poor situations to agree on national priorities.

In less donor-dependent countries, decision-making is less driven by outsiders, but is a highly political process, dependent on many different individuals and organisations pursuing, or negotiating to protect, their own interests. Individuals - whether scientists, public health professionals, politicians, heads of companies - all have different values which affect their behaviour. They have different competencies of persuasion, differently perceived status and power which influence the acceptability of their recommendations. The interviews conducted for the study were peppered with anecdotes of what a difference particular individuals had made at different stages of the decision-making process. What is clear is that decision-making is a *process* - not a one-time nodal point - in which many different actors play different parts, and which will be highly contextually specific to the culture, history and political system of each country.

The importance of networks of individuals in promoting new vaccines was a central finding in this study. Many interviewees mentioned the efforts or enthusiasms of particular people, attributing to them major policy shifts. Examples of such people given by a number of interviewees were Ciro de Quadros, seen to have had a major impact first in the Americas, later globally; Nakajima, as regional director of WPRO, seen as one of the important influences in getting HBV accepted in that region; Kane, as part of WHO was perceived as 'zealous' in his promotion of HBV. One interviewee suggested that change within countries was almost always due to one person, and gave examples of President Museveni in Uganda, who knew the immunization coverage rates for the country, and the President of Mali who actively promoted guinea worm control. Others referred to prominent parts played in supporting new vaccines by political leaders in the Philippines and Indonesia.

However, while few would quarrel with the notion that particular individuals may be central to change, their level of influence is determined by a number of different factors: their membership of informal and formal scientific and professional networks and their position in specific institutions. There were many examples of how close networks are in the vaccine field, by mapping individuals' moves between the major institutions involved (WHO, UNICEF, the World Bank), the Centers for Disease Control and Prevention (CDC), the Carter Center's Task Force on

Child Survival and the Task Force on Hepatitis B (now disbanded, and absorbed by the Bill and Melinda Gates Foundation/PATH Children's Vaccine Programme), the Children's Vaccine Initiative and the International Vaccine Institute, the Rockefeller Foundation and USAID-funded child survival projects. Many people have worked in two or more of these different organisations. Sometimes one organisation seconds or funds its own staff to work in other organisations. Informal and regular public-private sector contacts are also common. One interviewee mentioned that Merck and CDC do much work together on pricing and purchasing policy.

Institutional position is also important. Government leaders, for example, can pave the way for policy initiatives such as the introduction of new vaccines, and James Grant's name was often remembered by interviewees for his targeting of heads of state to promote child immunization. But institutional membership can also be used to block policy initiatives: several interviewees recalled an Indian official blocking acceptance of measles immunization. Institutions are also greater than the sum of their employees, and employees' actions are constrained or facilitated by institutional history, culture, vision, resources and the way they are perceived by others. To understand why and how, new vaccines become accepted, it is necessary to move away from individuals and their role in the decision process, and to look at the institutional effects on their actions. In this study we identified three broad themes which throw light on why new vaccines may not have been introduced on to the policy agenda:

- confusion over leadership
- negotiations over private-public links
- absent voices

Confusion over leadership

From the interview data it is clear that there is considerable confusion over which organisation is providing leadership in promoting new vaccines. Where once it might have been expected to come from WHO and UNICEF, both organisations are at junctures in their histories which constrain providing such leadership, but also there are other organisational actors interested to take the initiative.

In the 1970s and 1980s there was some tension between WHO and UNICEF in their interpretation of Primary Health Care (PHC), which both organisations had sponsored at Alma Ata in 1978. WHO's approach was to integrate and expand primary level services, with EPI as an essential part of PHC. UNICEF took a more selective approach, with immunization as part of Growth monitoring, Oral rehydration, Breast feeding, Immunization, and later Family planning (GOBI-FFF). Differences between the two organisations were to some extent overcome through the multi-partnered Task Force on Child Survival, and immunization against the six childhood diseases became a common goal for many countries and donors. With the international endorsement of Polio Eradication both organisations (and their donors) committed themselves to achieving this goal. WHO was perceived as providing policy guidance, UNICEF as being the funding channel and implementor of programmes.

In the 1990s the reputations of both WHO and UNICEF suffered. There was much criticism of WHO under its former Director General, and observers noted that the organisation had become dysfunctional, bureaucratized and ponderous; unable to make priorities and policy choices; and the staff were demoralised (Peabody 1995, Walt 1996). In this situation, there was poor communication and coordination on vaccines policy between WHO headquarters in Geneva and the regional offices, partly because there were only a few individuals at the centre with a remit to explore new vaccines' opportunities, and because most effort was being put into polio eradication. The regional offices of WHO fared no better than headquarters. There were few professionals

with a designated responsibility for immunization (let alone new vaccines) until concentrated effort was built up in the 1990s on the polio eradication campaign. Almost the only regional office to be mentioned positively in this context by all interviewees was PAHO, for its ability to provide leadership in the Americas on the inclusion of new vaccines. This must be seen in the context of successful immunization programmes in the Americas: by 1991 polio had been eradicated, followed rapidly by enhanced measles control. Surveillance systems established for polio were able to move on to gather information on the burden of disease (meningitis for example), a policy for HBV targeted to areas at highest risk was successful, and these efforts paved the way for the introduction of new vaccines into national systems. Such moves were facilitated by the strong inter-relationships established in the region between donors, PAHO and countries, the mechanisms for coordinating and promoting policy, such as the inter-agency coordinating committees, and a strong advocate in de Quadros, all of which were referred to by interviewees. None of the other WHO regions had this constellation of favourable factors.

However, with the appointment of a new Director General in WHO in 1998, many member states (and donors) believe that the organisation could be turned around, and regain its authoritative reputation in health.

Under new leadership after Grant's death, UNICEF has been perceived as searching for a new role, which remains unclear. This was apparent in the way many perceive its role in vaccines. During the 1980s, in spite of Grant's attempts to move UNICEF into support for research on new vaccines this was resisted by the Board (Muraskin 1998) and UNICEF's focus remained firmly on building national immunization infrastructures for the 6 original childhood antigens. With the change in procurement policy in 1994, towards targeting countries in the greatest need, countries which had depended on UNICEF had to make space in budgets for vaccines, and some interviewees thought that this may turn out to be at the expense of delivery systems. According to one interviewee, resources devoted to vaccines decreased from about $70 to $12 million (not counting polio vaccine) by the mid-1990s. The impression many respondents had was that UNICEF's policy position was very unclear. Indeed, a UNICEF interviewees' reply on being asked what the organisation's policy was on new vaccines was 'I wish I knew!'.

The Children's Vaccine Initiative, established in 1991, has had a troubled history, partly because of its original unclear and contested goals, but it is seen to have generated consensus around the need to invest in vaccine research, drawn attention to problems of vaccine quality and how to address them, and has stimulated WHO to think about its role in getting existing vaccines into developing countries (Muraskin 1998). Nevertheless, the CVI's ability to act has been undermined by its uneasy relationship with WHO and the perception that it is US-dominated. Many of the functions of CVI are similar to GPV, exacerbating the potential for duplication and competition. Outsiders are unclear as to which organisation has responsibility for what.

These organisations are strongly affected by their relationships with bilateral donor agencies who provide extrabudgetary resources for specific programmes. And it is clear from this study that European donors have been much more cautious than, for example, USAID, the only agency with a programme on new vaccines. Although no interviewees said so explicitly, this may be because donors want to demonstrate confidence in the new leadership at WHO, to support the new priority programmes, such as 'rollback malaria', and to give the restructuring of the organisation a chance to prove it can overcome former dislocations and divisions. It may also be the case that, in comparison with American agencies, both state and non-state, the European donors are less oriented to technological solutions and more concerned with the practicalities of sustaining health systems and infrastructures (Muraskin 1998; p152 quotes the Dutch on this point). Representatives from European donor agencies said that they were not against new vaccines, but

were reluctant to support what were often perceived of as vertical immunization programmes. Given current financial and political uncertainties and restrictions, and the push for health reforms, it is perhaps not surprising that European donors are cautious in supporting additional interventions in hard-pressed health systems. Many interviewees also stressed how important it was to guarantee sufficient funds to complete the polio eradication campaign.

Many of the interviewees saw the European donors' apparent disinterest as a barrier to the introduction of new vaccines. One interviewee said that Africa is not getting HBV because the donors are not buying HBV for donor-dependent countries, and several felt that the polio eradication campaign was being used as an excuse for not re-thinking immunization policies.

Finally, the role of CDC needs to be taken into account in understanding the apparent lack of policy clarity at international level. Although primarily aimed at improving the health of american citizens, and therefore mostly concerned about domestic immunization policy, CDC has, through its expertise and staff, exerted considerable influence in international health. It is only in the last decade that routine infant immunization schedules in the USA have included new vaccines, and according to some observers, CDC has not shown strong commitment to pushing for new vaccines in national immunization programmes in poorer countries. Advocacy and energy in CDC have been devoted to polio (and now measles) eradication, because of their importance for US citizens and thus their attraction of earmarked funds from Congress.

Negotiating public-private links

Cautiousness and lack of clear leadership on vaccines policy is, however, balanced against a real effort to negotiate the potential for links between public and private sectors, and to search for mechanisms of collaboration.

The World Bank, having entered the health field as the major financier in the 1990s, has shown considerable interest in promoting new vaccines, in bringing industry and donors together, and in exploring a new global mechanism for more effective promotion of new vaccines. The 1998 meeting called by President Wolfenson with chief executive officers from a number of pharmaceutical companies manufacturing vaccines, gave high visibility to new vaccines, and publicised the wish to explore links with industry. Wyeth-Lederle have since approached the Bank to explore the possibilities for expanding globally through the introduction of a rotavirus vaccine. The Bank has held a number of consultative meetings at the national and international level to explore the support for a global coalition on new vaccines, and has hired staff who are expert in the vaccine field. The Asian Development Bank has also made new vaccines a priority for lending. It is not clear, however, that many countries have used loans to introduce new vaccines into immunization systems, despite the Banks' interest.

Other private-not-for-profit sector organisations in the US have been supportive of new vaccine promotion, and many interviewees mentioned Rockefeller's role in helping establish CVI, and PATH's role in promoting HBV at country level - particularly in Indonesia and Thailand. Towards the end of the research (on December 2 1998) the Gates Foundation and PATH announced the establishment of the Bill and Melinda Gates' Children's Vaccine programme (CVP), initially targeting four vaccines - rotavirus, Hib, pneumococcal and hepatitis B. The new CVP has stressed its independence, its willingness to work with others, and has pledged that it will not supplant the activities of WHO, CVI, UNICEF or the World Bank. History suggests that it will not be easy to adhere to this aim.

Partnerships between the private sector and international organisations as epitomised by the CVP are rapidly becoming a feature of the health landscape. Renewed interest in the USA in emerging

infections in the late 1980s led to structured meetings between industry and other actors in the health field (researchers, professionals, practitioners, governments) arranged through the Institute of Medicine (1997). The promotion of tiered or segmented marketing for vaccines (as introduced through the Batson-Evans grid) and the Mercer Report for UNICEF (CVI, 1994b) has been welcomed by industry, as was the UNICEF decision to allow discounted vaccines procurement only for those countries in greatest need. One industry interviewee said that tiered pricing demonstrated to industry that companies could make profits in the third world.

While there may have been some alleviation of the traditional distrust between public and private sector actors, interviewees mentioned a number of continuing tensions and concerns. Among these were the fact that the public sector interest is in developing single dose vaccines and combination vaccines, whereas industry prefers multi-dose and single vaccines; that industry is reluctant to talk only about driving prices down, but wants talks about 'adequate pricing'; that there are continuing industry reservations to transfer technology, with discussions about quality dominating negotiations; that some companies use questionable methods to obtain contracts and promote products. As one interviewee said, at the basis is a core debate on values between private profit and public goods.

At the country level, there are few links between private and public sectors. Private sector health providers at the country-level are reported to offer a wide range of vaccines, sooner than the public sector as they have few barriers beyond national licensing to overcome and a ready market for the product. Madrid (1998a, 1998b, 1998c) found the impact of private sector vaccine use highly variable between countries, but "neither necessary nor sufficient" to cause national introduction of a vaccine. Its primary function has been to provide governments with a chance to familiarise themselves with, and potentially catalyse interest in, new vaccines prior to national adoption.

Absent voices

Interviews were conducted with actors working at the international level, and the views from countries will be ascertained in a second phase of the study. However, when asked to suggest reasons for slow adoption of new vaccines, it was remarkable how few of those interviewed mentioned the problems being experienced at the country level: basic health systems breaking down, financial exigencies leading to reversals in policy (for example, the planned introduction of Hib in South Africa and Thailand became impossible after the Asian financial markets crashed, resulting in a rise in exchange rates). A few interviewees drew attention to decision-making processes, suggesting that nationals had considerable difficulties getting their voices heard. The perception of one interviewee was that discussions at WHO and CVI were dominated by the Americans and Europeans, and that because meetings were conducted in English, participants from developing countries were often at a disadvantage, even despite translation.

Several people mentioned the influence of WHO and UNICEF at the country level, the former for its expertise and standard-setting, the latter for its financial support, but also its promotion of Universal Child Immunization. There was a suggestion that, because countries had depended on UNICEF for policy advice and assistance on immunization during the UCI years, UNICEF'S lack of interest in introducing new vaccines had led to their low priority in national programmes. Further, some interviewees suggested that because countries had received vaccines free, they were now perceived by some national authorities as a public good which ought to be provided without cost to the country. The World Bank was also perceived to have a sometimes 'overpowering' presence in countries, although it is not clear that the Bank has played much role at the country level in getting new vaccines into policy agreements.

Many talked about the importance of identifying a national (or regional) champion for getting action on a specific vaccine, and the obverse - when there was no-one in a country taking specific responsibility for a particular vaccine (or disease), then neglect occurred. This was compounded by the lack of information on disease burden or need, common to many poor countries. Among our interviewees, the lack of an advocate was the explanation most often proffered in relation to the neglect of immunizing against yellow fever, although the nature of the disease was seen to be a factor too. Among those few interviewees who talked about country level decision-making, there was consensus that if key decision-makers did not perceive the disease to be a priority, or did not consider that a feasible approach to vaccine introduction existed, then it was not likely that the country would change its current immunization policy. On the other hand, it was clear that a strong policy champion could over-ride policy inertia or disinterest.

Policy environments at the national (and regional) level differ, and interviewees drew attention to the need to know the country well in order to identify key decision-makers, one person noting that industry was usually adept at this. In some countries the most influential policy-makers are not in Ministries of Health but in Finance or Planning; in others, business leaders are highly influential, and have access to key government officials. Muraskin's study on getting HBV into Thailand and Indonesia (1995) confirms these views. However, identifying the appropriate policy-makers is only one step in policy development. Windows of opportunity shift as ministers and top civil servants are moved within the system (or out of it), or programme managers are attracted out of government jobs into private sector or international organisations. Donor country office personnel also change, and with relatively short budget cycles and shifting policy priorities, sustaining and advocating changes in policy can be difficult.

In summary, the data suggested three explanations for perceived caution in introducing new vaccines into national immunization programmes. First, there is no clear consensus or leadership at the international level, among those agencies policy-makers would be traditionally looking to. Second, while there is general support for the attempts being made to find mechanisms for collaborating with industry, difficulties in reaching agreements and continuing concerns about public-private governance make this a slow process. And finally, insufficient space has been allowed for national views to be expressed, and too little is understood about policy-making environments.

5. Concluding discussion

The findings from this study, and others, suggest that a number of different explanations are helpful in considering the process of adoption of "new" vaccines (specifically HBV and Hib) and "old" vaccines (yellow fever). While decisions to introduce new vaccines are not merely economic, procurement financing and economic constraints have played a major part in determining whether new vaccines are introduced into NIPs. There is no doubt that HBV was slow to be accepted until the price declined in the early 1990s. Further, new vaccines have been developed in an environment of considerable uncertainty in global financial markets and political systems, which have gravely affected health systems undergoing major structural and financing reforms. Indeed, the analysis from this study throws some doubt on the perception that adoption of HBV and Hib has been slow, suggesting that, on the contrary, given a highly difficult policy environment internationally and in many countries, adoption can be seen to be progressing relatively rapidly. The themes that follow illustrate some of the difficulties faced at the international and national level in deciding whether or not to include new vaccines in existing immunization programmes.

- adoption of new vaccines is part of a political process and takes time
- there is confusion over vaccine priorities and policies
- policies on vaccines are supply-driven not demand-sensitive
- varying perceptions of 'affordability' lead to inconsistent policy positions
- technical problems have been underplayed
- advocacy is more influential than any other factor in facilitating change

Adoption of vaccines takes time, but is not always slow

One of the concerns driving this study was that countries have been slow to adopt new vaccines, and that existing vaccines such as yellow fever have been neglected. While the latter is certainly an issue in those countries where yellow fever continues to affect significant numbers of the population, it is less clear that progress has been tardy in relation to new vaccines.

Measles vaccine was licensed in the USA in 1963, yet it took over 20 years to get it introduced in Asia. Measles coverage continues to be low in West and Central Africa where mortality is highest. Thus the apparent slow introduction of HBV is not surprising. New vaccines have been introduced into routine infant immunization programmes in the USA only in the last decade, and HBV is still not part of routine immunization in the UK. Hib, for example, is being rapidly absorbed into NIPs in Latin America, and it seems that other parts of the world are moving ahead too - according to information from EMRO and WPRO. Given the difficulties of measuring the burden of disease from this infection, and the high costs of the vaccine, this is particularly impressive.

However, while it may be hasty to conclude that countries have been sluggish in adopting new vaccines, there does appear to have been a major failure with yellow fever. The study provided many different insights into why this has been a lower priority vaccine, ranging from a historical drop in scientific interest in arboviruses (influenced by the hiatus in funding after Rockefeller shifted priorities); the 'hidden' nature of disease - one interviewer suggested it was an 'out of sight, out of mind' disease; no clear case definition; poor laboratory facilities; many unanswered technical questions over strategies; its relative lower priority in the face of major, highly visible problems such as meningococcal epidemics; and no clear advocates at country, regional or international level (although this may now be changing). It seems that WHO may have missed opportunities in the past, and has not always fulfilled its normative role in identifying technical

issues around vaccines (for example giving practical advice early on to managers on the timing of doses when including HBV in EPI schedules); and that it has not always acted in a timely fashion, to catalyse action in vaccine-neglected diseases such as yellow fever.

A confusion of priorities and policies has affected vaccine uptake and financing

There has been no clear and consistent international message to say that new vaccines are a high priority. The vision and consensus, mediated and catalysed through international champions such as James Grant, Albert Sabin and Jonas Salk which characterised immunization programmes in the 1970s and 1980s, has dissipated. However, the study found that attributing any confusion over policy or lack of consensus on the value of new vaccines to 'lack of political will' is simplistic. The decision-making process is itself complex and there is genuine uncertainty about what policy approaches are best in the long term. Interviewees were divided, and the international community often takes polarised positions, on whether it is best to assist countries through specific disease-control programmes or through building up health infrastructures.

There are real dilemmas facing both donors and national policy-makers in choosing between many multiple and competing policy and funding priorities. This is perhaps most stark in the case of Africa, with some of the poorest countries in the world. Donors are being urged to support the completion of the polio eradication campaign (acknowledged to be in the most difficult and expensive final phase), and increasingly, the elimination of measles; to fund 'roll-back malaria'; and to continue to assist in the AIDS epidemic. Many are acutely aware of the problems of sustainability in the face of experience gained in the 1980s with vertical programmes. At the same time, donors are trying to give countries incentives to continue structural and financial reforms to health systems, whose infrastructures are increasingly under threat. Further, in order to bring coherence to the use of external resources in the health sector, many donors are promoting Sector Wide Approach Programmes (SWAPs), the establishment of which demands considerable resources of time and money.

However, donors themselves are involved in the process of decision-making at the international level, and it is the multi and bi-lateral agencies themselves which put all these different and competing potential programmes on the policy agenda**,** as reflected in their financing of GPV (See Table 4). In other words, there is considerable confusion, and therefore inconsistency and a lack of coherence in the international community about which priorities, and which approaches are best. What seems clear is that where bilateral donors once supported WHO (and UNICEF) policies on immunization, this is no longer the case. Bilateral donors themselves have greater technical expertise than they once had, have a great deal of experience in implementing programmes, and look to the World Bank at least as often for policy advice. WHO and UNICEF are undergoing some organisational transition, and it may take time for authority to be re-established and priorities clearly enunciated.

The extent to which bilateral donors can influence WHO's policies is illustrated below. A review of GPV financing shows that donors provide over $20 million of the $23 million total funds for GPV, and of these extrabudgetary funds, 56% go to ear-marked, donor-specified projects.

Table 4: Donor Influenced Funds in GPV Global Budget, 1998

WHO Regular Budgetary Allotments	**$3.4 million**
Extrabudgetary Funds	
Specified by donors for specific projects	**$11.4 million**
Designated by Donors for specific unit of GPV	$ 3.8 million
Unspecified-Use at discretion of GPV	$ 5.0 million
Total Extrabudgetary Funds	$20.2 million
Total GPV Global Funds	**$23.6 million** *(GPV, 1998d)*

While WHO is often criticised for its lack of leadership in priority setting, it is clear that it is, at least to some extent, limited in its choices, and existing competition between the various international agencies does not help to reach consensus on priorities. Within WHO it is GPV which should be helping to establish global priorities, although the division can only do this if it is recognized by other agencies as having this normative role, and it is unclear that this is the case. CVI may well see its role as one of leadership, and unless contradictory perceptions are clarified international coherence will continue to be a problem. Currently polio eradication, measles control, vaccine research and development, and HBV are GPV's biggest priorities. "New vaccines" are one of GPV's strategic objectives, but the emphasis is on "filling the vaccine pipeline," not introducing available new or underutilised vaccines into NIPs.

Table 5 aggregates the funds allocated to any aspect of new vaccine introduction in GPV's 1998 global budget. At most, 13.1% of funds go to support such things as disease burden studies, vaccine trials, and investigations of financing mechanisms which facilitate the introduction of new vaccines. This total includes funds for vitamin A supplementation, so the actual allocation to new vaccines alone is somewhat lower (GPV, 1998d). Funding patterns at GPV reflect the priorities it establishes in its normative role, for the global community, but also the wishes of donors, who ear-mark their extrabudgetary contributions for particular diseases or activities.

Table 5: Elements Pertaining to New Vaccine Introduction in the 1998 GPV Global Budget (All identifiable, relevant areas, including surveillance.)

	% of GPV Budget	**Actual Amount US$**
Hib	3.8%	892,000
Hepatitis B	2.4%	568,000
Yellow Fever (Including Micronutrients)	5.7%	1,356,000
Rubella	0.5%	129,000
General Support of New Vaccines	0.7%	167,000
Subtotal New Vaccine Introduction	**13.1%**	**3,122,000**
All Other Budget Items	86.9%	20,478,000
Total GPV **Global** Budget	100%	23,600,000 ***(GPV, 1998d)***

Finally, there has been a huge increase in private sector activity in the vaccine field - from a (much welcomed) increase in industry interest in vaccine development and promotion, to new partnerships between private and public sectors. Multiple actors, with diverse interests makes reaching consensus a more complex process, and can exacerbate the difficulties in agreeing on priorities at the international level. Establishing priorities is more difficult in conditions of uncertainty over funding, and this is another characteristic of the current policy environment. With the change in UNICEF's policy and financial support for vaccine procurement, the World Bank has been playing a major role in consultations over the possibility of establishing a global financing initiative for new vaccines, although the outcome of these meetings, and any impact on the future of vaccines is as yet unknown. The increased activity of the vaccine industry in marketing and supply, and more active negotiations between private and public sector organisations over prices and strategy increase uncertainty. At the country level policy-makers may be faced with a barrage of often conflicting advice and assistance and priorities are especially difficult to decide on in highly-dependent countries, where choices are particularly stark.

Policies on vaccines are supply-driven not demand-sensitive

Although the study did not look at decision processes at the country level, from interviews and other studies asking what was understood about national policy processes, it seemed that in the past vaccine policy has largely been decided by international experts and donors, and that few countries (or regions) have a clearly enunciated policy on the introduction of new vaccines into NIPs. This is partly a reflection of the way international agencies behave. Many emphasize international actions in promoting new vaccines, as opposed to their use in NIPs. Thus the focus is on ensuring the availability of new technologies and antigens, guaranteeing that manufacturers are producing adequate quantities of vaccine of known quality, and developing research data sufficient to justify international recommendations for use. However, as past willingness to pay for vaccines, and, to some extent, infrastructure, have declined, the point of decision has shifted to the country level. Increased responsibilities for funding, decision-making and integrating new vaccines are now being put on countries. Some interviewees noted with satisfaction that the changes in procurement policy for vaccines meant that those countries not 'in greatest need' had to introduce vaccines as line items in budgets, and one noted that by so doing, new vaccines such as HBV had been protected at times of financial crisis (as in Thailand).

However, if countries are expected to take greater responsibility for the introduction of new vaccines, then international agencies will have to be more demand-sensitive. Country demand and willingness to commit resources, not solely international pressure on the supply side, will be essential features in any expansion of NIPs. While informants to this study identified examples of economic exigencies curtailing or postponing new vaccine adoption at the country level, it is clear that financial decisions are by no means the only, or even necessarily the most important factor in the decision-making process. Likewise data on disease burden or cost-effectiveness (often missing) might or might not influence policy change. Personal experiences, enthusiasm, self-interest, position, were all mentioned as important influences in particular decisions. One interviewee described country level decision-making as 'non-linear, but not ad hoc'. Further, the study's findings suggest that decision-making processes differ from country to country and region to region. PAHO's linguistically homogeneous region, with many different established and respected mechanisms for policy discussion and interchange, seems to facilitate policy transfer, leading to rapid adoption of new policy after successful demonstration in one or two countries. Appendix 7 summarises the factors that appear to affect decision-making on new vaccines at country compared to international levels.

However, it must be emphasised that the data that informed this study was gained largely from an international network of scientists, professionals, and academics, and that country level voices were absent. The report does not presume to speak for developing country decision-makers, from whom only limited data was collected at this stage.

Cost as a barrier to introducing new vaccines and to questions of equity

Findings suggest that 'affordability' is a contested concept. For many countries' public health systems, new vaccines remain relatively expensive. Even with decreased costs, prices are a much higher percentage of GDP in developing than in developed countries, and costs of research and development, production and regulation are increasing. It is clear that the prices of new vaccines will not fall anywhere near the low levels of the original six EPI vaccines.

The perception of 'affordability' is central here. For developed countries, even expensive vaccines may be good value, if seen as an investment in the future. The significant level of resources necessary to complete polio eradication is worthwhile to the industrialized world because of the huge benefits it will bring. For developing countries, however, especially low-income countries, the costs are considerable (even where many of the resources are external), and of less importance than other pressing disease problems. In developing countries, the fixed costs of EPI are about $14, while the original 6 vaccines cost approximately $1 in total. Additional antigens cost between $0.5-3 *per dose*. Even allowing for price tiering for poorest countries (so that they pay only 20% of the market cost of vaccines) new vaccines continue to make up a much larger percentage of per capita GDP than in industrialised countries.

'Affordability' is juxtaposed against the moral imperative that 'all the world's children, regardless of socio-economic level, have the moral right to receive the benefits of life-saving vaccines' (Presentation to press at Gates' CVP launch, 1998). However, some donor representatives interviewed questioned the rationale for adding new vaccines to struggling NIPs, where infrastructures were weak and coverage low. They argued that effort and resources were best spent on the 6 childhood diseases and supporting existing NIPs. Others recognised the potential threat to equity of this approach - the poorest countries with weakest infrastructures may never then receive new vaccines, and have to cope with the costs of resulting disease in already overstretched health services. They saw new vaccines as an opportunity to reinforce infrastructures, and to boost the coverage of the 6 original antigens, as well as lessening the costs borne more directly by countries (hospitalizations, growth retardation, parents' lost worktime and so on).

As said, there is considerable inconsistency in donor views: many low income countries are almost entirely dependent on donors for drugs, of which vaccines are a very small percentage - and while adding new vaccines would certainly raise the costs, they have a strong public good benefit which is less true of other drugs. Further, yellow fever vaccine is beginning to be supported in some African countries, even where coverage rates are below 50%.

Neglect of technical questions in the introduction of new vaccines

In the enthusiasm to make new vaccines available to larger numbers of people, it may be that some difficult technical questions have been overlooked. For those concerned with actual delivery of programmes at the country level, this may be a strong factor in waiting to see how policy and strategy develops in relation to new vaccines before their inclusion in NIPs, which on the whole, have solved problems of dosage, timing, cold chains and so on for the original 6 antigens. Many countries still need better epidemiological data to help decide how far new vaccines are in the public interest; the possible need to demonstrate protection against serotypes prevalent in that country; confirmation of the efficacy of the vaccine (particularly for Hib and the newer

pneumonia and rotavirus vaccines); the need to develop optimal dose and time schedules. If EPI managers do not have clear guidelines on how much, and when to deliver new vaccines, and how to monitor their impact, they could be a force of resistance to its introduction. In this respect, some interviewees noted the importance of follow-up of global recommendations by practical guidance at the country level. For Yellow Fever, despite recommendations for its use, very little time was devoted to preparing plans for its introduction or discussing difficulties during inter-country workshops. Action to rectify this began in 1998 but continued monitoring and review will be needed.

Advocacy is more influential than any other factor in facilitating change

An effective advocate or champion can be more influential in facilitating vaccine adoption than any other factor, particularly at the country level. Numerous interviewees noted the current absence of strong and highly visible global vaccine advocates. The importance of advocacy within an agency for building up support in a programme of work, and having one or two individuals within the agency with sufficient authority and leeway to persuade others - whether groups or individuals - was mentioned by many. There were many anecdotes relating the influence of one advocate at the country level, including political leaders who had a personal or familial experience with the disease, leading to their commitment to a vaccine's introduction. Interviewees reported from their own experiences, examples where advocates had overcome obstacles of perceived high cost or lack of data on illness, and facilitated the decision to introduce a new vaccine. The annual summit of First Ladies in Latin America was noted to have been used as a good venue for Ciro de Quadros to update key figures on what was happening in immunization. EPI managers were noted to have been particularly effective in Zimbabwe in pressuring for new vaccines, and many admired the effort by WPRO to lobby for vaccines. Alternatively, there was recognition that advocacy was not always used in a positive way, and examples were given of where industry representatives had used bribery or dubious marketing techniques to push a particular vaccine or to build up public fear about a disease.

6. Recommendations

1. Advocacy is essential, and long term strategies should be devised to explore a number of ways of facilitating change, for example by:

- identifying champions or advocates at the international, regional and national level
- gaining the interest and support of top politicians such as ministers of health, heads of state or key figures in the business community
- working with parliamentary committees to get legislation on immunization
- ensuring budget lines for immunization
- finding committed health professionals, creating informal and formal networks of advocates
- initiating study tours to enthuse professionals and/or policy-makers
- holding 'in-family' meetings (to discuss technical issues, to build and sustain interest)
- making long-term strategies to identify and train key professionals in specific diseases, techniques, programme management and evaluation
- undertaking burden of disease, cost-effectiveness studies to provide information for decision-making
- using vaccine introduction to improve information and surveillance systems

2. The format of information and the position of spokespersons conveying data on new vaccines is
   as important as the content, and consideration should be given to identifying the most effective messengers for promoting commitment to new vaccines at the international level and in countries and seeing that information and data is available to all relevant decision-makers and managers.

3. Particular effort needs to be made at the international level to resolve differences and inconsistencies in vaccine policies, with clearly demarcated functions for different organisations. The potential for overlap and duplication between CVI, GPV, Bill and Melinda Gates Foundation's CVP and the World Bank's vaccine financing initiative group should be addressed. Differences between European donors and others also need to be addressed. Leadership and coherence needs to be revived.

4. International organisations should be assisting countries to set priorities for immunization, develop plans of action, and plan ways of raising funds. These activities should be geared to individual country circumstances, political and health systems, and be undertaken with key policy-makers. This implies that different strategies will be employed in different regions so that varying needs and priorities can be taken into account.

5. The introduction of new vaccines should be used to reinforce and support existing infrastructures. Funds for new vaccines therefore have to include resources for training, surveillance, monitoring and evaluation systems. Statements suggesting that new vaccines should be made available only for those countries with over 70% coverage rates should be re-visited, taking equity into consideration.

6. Funds for new vaccines must be generated, without prejudicing the polio eradication campaign's completion. Discussion and research should be conducted to explore and compare alternative approaches to financing: the use of World Bank loans, a global endowment plan, the bulk purchase of vaccines and revolving funds, and to assess their impact on NIPs and the wider health system.

7. International organisations should improve their understanding of decision-making processes at the country level, strengthen mechanisms for getting nationals' voices heard and expressed, work with nationals in data collection, burden of disease studies and other sources of information to build knowledge and national constituencies for policy change.

8. Attention should be paid to translating international policy advice into practice, by devising practical guidelines to help managers incorporate new vaccines, and applied research should be supported in order to continue solving some of the technological concerns around dosage, timing and immunization schedules. Follow-up of policy recommendations by practical action in the field is essential.

9. The positive experiences from PAHO and WPRO in the promotion of new vaccines should be shared across regions, and regional offices should provide support to countries in their decisions about incorporating new vaccines into NIPs. This may be through helping to develop plans in conjunction with national NIP and or EPI staff, akin to the YF plan of action, which should include programmatic, as well as funding/sustainability, and advocacy objectives; or it may be through support for disease burden and cost-effectiveness data where helpful to country decision-making; or it may be through regional offices' promoting regional exchanges of experience.

10. In order to facilitate debates and reach consensus on national and regional priorities, the potential conflict between eradication programmes and introduction of new vaccines needs to be clarified. In strong regions eradication programmes have apparently enhanced the ability to introduce new vaccines. In weak regions, there are anecdotal reports of the opposite. Before further eradication programmes are embarked on, clear strategies must be developed to ensure that these do not hinder introduction of new vaccines in low income countries.

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Appendix: 2

Major Statements on New Vaccines

1987 Global Advisory Group

"Hepatitis B immunization programmes should primarily aim at the prevention of chronic carriage of hepatitis B virus and should be considered in all population groups with chronic carrier rates of hepatitis B virus of over 2%; they become a major public health priority for populations with carrier rates above 10%.

Countries with chronic carrier rates of hepatitis B of over 2% and with resources to initiate and sustain hepatitis B immunization programmes should introduce hepatitis B immunization as an integral part of existing childhood immunization programmes."

Source: EPI, 1990

World Health Organisation: 45th World Health Assembly Resolution on Immunization and Vaccine Quality (1992)

> "Urges Member States:…to integrate cost-effective new vaccines, such as hepatitis B vaccine, into national immunization programmes in countries where it is feasible."
>
> "Yellow fever vaccine should be routinely administered to children under one year of age in all countries at risk of yellow fever by 1993;"
>
> "Hepatitis B vaccine should be integrated into national immunization programmes in all countries with a hepatitis B carrier prevalence (HbsAg) of 8% or greater by 1995 and in all countries by 1997. Target groups and strategies may vary with the local epidemiology. When carrier prevalence is 2% or greater, the most effective strategy is incorporation into the routine infant immunization schedules. Countries with lower prevalence may consider immunization of all adolescents as an addition or alternative to infant immunization."

1995 SAGE Report (WHO/GPV/95.05)

> "The first priority for vaccine supply and financing is for the existing 'core' vaccines. The introduction of new vaccines which have been identified by CVI/WHO as a priority will be dependent on an assured supply of these vaccines. Financial support for new vaccines will be contingent on the sustainable supply of existing vaccines as well as on the following priority-setting criteria:
>
> - Financial need (Band A)
> - Sustainable financing of existing vaccines, with the government meeting their targeted self-financing level;
> - Magnitude of health risk;
> - Programme ability to include another vaccine (measured by coverage); and
> - Priority placed by the Ministry of Health on introducing the vaccine.
>
> The weighting of these criteria will depend on the specific vaccine and its impact on controlling disease. For example, yellow fever will be supported for all countries at high risk for the disease, but hep B vaccine will be supported for countries at a higher risk (greater than

5% HbsAg) and with strong programmes (DTP coverage greater than 70%). The low coverage programmes would be encouraged to focus on strengthening their existing infrastructure and delivery of the current vaccines. Government will be assisted to access the new vaccines once 70% coverage is reached." (Page16)

UNICEF/WHO State of the World's Vaccines (1996)

"UNICEF has made it clear that support for new vaccines for countries in bands A and B will not be automatic. Priority will be determined on the basis of four main criteria:

- financial need;
- the magnitude of the health risk;
- the ability of the national EPI to deliver other vaccines; and
- government commitment to sustain their national immunization programmes.

Moreover these criteria will each be weighed according to the specific vaccine and its potential impact in the country involved. The purchase of YF vaccine, for example, will be supported for all high-risk countries while purchase of hepatitis B vaccine will be restricted to high risk countries that also have high rates of immunization coverage for other vaccines. For hepatitis B vaccine, the criteria are hepatitis B carrier rate of over 5% of the populations plus immunization coverage of not less than 70% coverage with three doses of DTP vaccine.

The remaining countries in bands C and D, which have demonstrated their ability to become self-sufficient in financing their vaccines needs, will be expected to go it alone-negotiating directly with vaccine manufacturers to obtain an 'affordable' tiered price for new vaccines." (Page 14)

"The outcome of efforts to finance new vaccine will hinge on the success of four key strategies:

- Targeting donor support to the neediest countries;
- Tiered pricing by manufacturers;
- A commitment by governments and donors to increase the amount they now spend on vaccines; and
- Advocacy to encourage governments, donors, and the general public to recognize the value of vaccines on the basis of their health impact in individual countries." (Page 23)

1996 SAGE Report: WHO/GPV/96.06

"In order to have a sustainable base for new vaccines, every government should finance the cost of existing EPI vaccines for routine immunization to at least the minimum level indicated by the WHO/UNICEF vaccine targeting strategy.

Countries must become increasingly responsible for financing the introduction of new vaccines. Donor funding should be coordinated and targeted to the neediest countries.

Tiered pricing is critical to the introduction of new vaccine. The SAGE strongly endorses the market segmentation strategy…

GPV should work with financial institutions such as the World Bank, other development banks, and donors to include immunization coverage, an indicator of 'allocative efficiency' (largest impact for money spent) and commitment to equity as a criterion for development lending and grants. The donor community, including development banks, should also be

increasingly involved in exploring the potential of immunization and the strategies and funding needed to achieve this potential.

Top priority should be given to efforts which increase the perception of the value of vaccines, among governments, donors and agencies…" (Page 28)

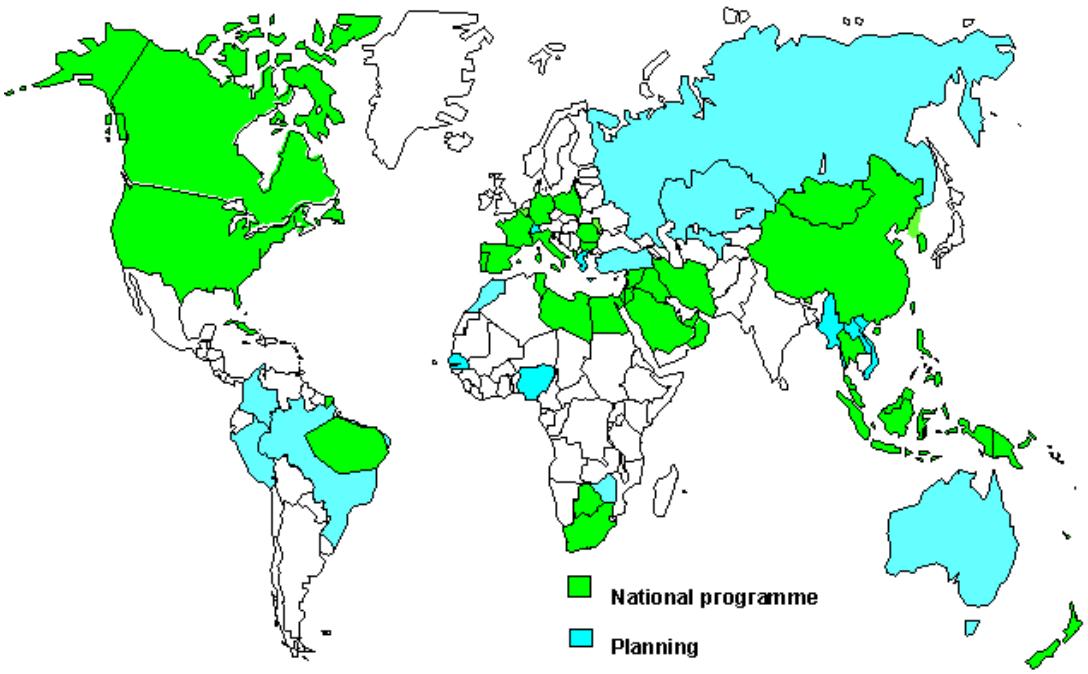
1997 SAGE Report (WHO/GPV/97.05)

"In view of the demonstrated safety and efficacy of the Hib conjugate vaccines, Hib vaccine should be included, taking into account national capacities and priorities, in routine infant immunization programmes. In geographical regions where the burden of Hib disease is unclear, efforts should be made to evaluate the magnitude of this health problem."

Appendix 3: Framework for Evaluating a Vaccine for the EPI (WHO/EPI/GEN/93.5)

Questions to consider prior to recommendation for inclusion
Priority of the diseases and its control • Definition of the problem • Magnitude of the problem • Strategies to address problem • Immunization versus other interventions • Cost-effectiveness
Characteristics of the vaccine • Immunogenicity • Efficacy • Duration of immunity • Interaction with other antigens • Safety/adverse reactions • Dose • Route of administration • Storage • Thermostability • Potential for combination with other antigens
Programme feasibility • Impact on immunization programmes • Impact on distribution systems • Cultural acceptability
Vaccine Supply • Technology transfer • Impact on local production • Adequate global supplies • Affordability

Appendix 4: Countries Implementing Routine Childhood Hepatitis B Immunization 1997



(Source: http://www.who.int/gpv-surv/graphics/htmls/hepb.htm, Jan, 1999)
Data as of April 1998

Appendix 5: Status of *Haemophilus influenzae* type B vaccine use as of December, 1998

WHO Region	Country	Hib immunization policy	Planning to implement Hib immunization policy	1997 Hib Coverage (%)
AFRO	Gambia	yes		
AFRO	South Africa		Planning for 99	
AMRO	Argentina	yes		
AMRO	Brazil		Planning for 99	
AMRO	Canada	yes		
AMRO	Chile	yes		
AMRO	Colombia	yes		
AMRO	Costa Rica	yes		
AMRO	Mexico		Planning for 99	
AMRO	Peru	yes		
AMRO	Puerto Rico	yes		
AMRO	Uruguay	yes		
AMRO	US Virgin Islands	yes		
AMRO	USA	yes		
EMRO	Bahrain	yes		
EMRO	Kuwait	yes		
EMRO	Oman		Planning	
EMRO	Qatar	yes		
EMRO	Saudi Arabia		Planning	
EMRO	Syrian Arab Republic		Planning limited implementation for 99	
EMRO	United Arab Emirates		Planning for 99	
EURO	Austria	yes		90%
EURO	Belgium	yes		6%
EURO	Denmark	yes		92%
EURO	Finland	yes		
EURO	France	yes		
EURO	Germany	yes		
EURO	Iceland	yes		
EURO	Ireland	yes		
EURO	Israel	yes		93%
EURO	Luxembourg	yes		86%
EURO	Netherlands	yes		95%
EURO	Norway	yes		
EURO	Spain	yes		
EURO	Sweden	yes		
EURO	Switzerland	yes		
EURO	UK	yes		95%
WPRO	American Samoa	yes		
WPRO	Australia	yes		
WPRO	F. States Micronesia	yes		
WPRO	Fiji	yes		
WPRO	New Zealand	yes		86%
WPRO	Palau	yes		
WPRO	Samoa	yes		
	Total # of countries*	**30**	**14%**	

*Total does not include territories reporting to WHO
Source: Dr. Jay Wenger. 12/1998 CVI/GPV. Geneva.

Appendix 6: Yellow fever outbreaks, immunization coverage & performance in African countries at risk for yellow fever outbreaks

County	Total reported cases 1982-1996	Last time cases Reported	Reported at least one outbreak 1982-1996	<50% immunization coverage*	YF vaccine included in the EPI (even partially)	YF imm. coverage (latest year)	Measles imm. coverage (1997)
Angola	37	1988	+	+	+	34 (1997)	78
Benin	142	1997	+				82
Burkina Faso	280	1985	+	+	+	27 (1997)	68
Burundi							50 (’96)
Cameroon	184	1994	+	+			43
Cape Verde Is.							82
CAR				+	+	28 (1997)	46 (’96)
Chad				+	+	28 (1994)	30
Congo		1961					18
Eq. Guinea		1970					82
Eritrea				+			53
Ethiopia		1966		+			52
Gabon	44	1995	+		+	23 (1991)	57 (’96)
Gambia		1979			+	91 (1997)	91
Ghana	523	1996	+		+	28 (1996)	59
Guinea	5	1987	+				56
Guinea Bissau							51
Cote d’Ivoire	25	1982			+	59 (1997)	68
Kenya	64	1995	+	+			32
Liberia	360	1997	+				44 (’96)
Mali	305	1987	+	+		3 (1994)	56
Mauritania	21	1987	+	+	+	32 (1990)	20
Niger		1939		+	+	27 (1995)	42
Nigeria	20,337	1994	+	+	+	1 (1993)	69
Rwanda							66
Sao Tome						2 (1994)	60
Senegal	79	1995	+		+	46 (1994)	65
Sierra Leone	33	1995	+				28
Somalia							…
Sudan		1942					92
Tanzania							69
Togo	7	1987	+			14 (1993)	38
Uganda		1971					60
Zaire (DR Congo)		1972		+		8 (1992)	20

* = designated as in greatest need of improved programme performance and enhanced financial support (EPI Information System, 1997)

Reproduced from GPV, 1998a

Appendix 7: Summary factors impacting vaccine introduction identified by the international community *

International Level	**Factor**	**Country Level****
Financing mechanisms Donor funds available Competing priorities	Cost	Perceived affordability Financing mechanisms Budgetary commitment **Economic outlook/currency stability** Competing priorities
Integration with EPI schedule	**Programme Feasibility**	Impact on EPI infrastructure Strength of EPI
Efficacy Effectiveness Cost-Effectiveness	Data	Perceived disease burden/severity Affected population groups Efficacy? Effectiveness? Cost-Effectiveness?
WHO? Global level advocates Industry NGO's/Foundations	**Advocacy**	WHO? WHO Regional Offices? National level decision-makers Industry NGO's/Foundations
Donor support Measurable outcomes/impact Competing priorities Support of key actors	Sustained Will	Perceived need/demand Perceived vaccine benefits Champion Rapid, visible results Competing priorities Socio-cultural belief system Public support Media coverage Support of key actors: Pediatric community Academia
See Appendix 3	**Vaccine Characteristics**	Availability of combination vaccines See Appendix 3
	Previous experience with a vaccine	Private sector Trials/Demonstration projects Epidemics/outbreaks
Multiple suppliers Sufficient quantity available Vaccine of known quality	**Supply/ Manufacturing**	Multiple suppliers Sufficient quantity available Vaccine of known quality Impact on domestic manufacturers

* **"Factors are complementary to those identified in Appendix 3".**

****Data reflects the views and perceptions of key informants at the international level of factors felt to be important at the country level. It should not be considered to represent country-level views.**