Executive summary

Introduction

1) The meeting was held on 31 January 2000 in Davos during the 30th World Economic Forum.

2) Dr Gro Harlem Brundtland, Director-General of WHO and Chair of the Global Alliance for Vaccines and Immunization (GAVI) Board, discussed the WEF panel session launch scheduled for later in the afternoon (see Annex 5) and introduced the Agenda and main aim of the meeting. She also referred to the resolution recently adopted by the WHO Executive Board regarding the Alliance (Annex 6).

3) Tore Godal, Executive Secretary of the Alliance, then gave a brief overview of the progress and challenges of the Alliance (Annex 1).

Increasing access and strengthening infrastructure

4) The main point on the agenda was to discuss the Alliance strategy for increasing access and strengthening infrastructure based on the working document "Immunize Every Child". In this context the Board emphasized the following:

- Improving access and infrastructure is not only a matter of finances but a significant managerial challenge; capacity strengthening is crucial in building sustainable immunization services.
- Immunization costs per child increase as countries approach 100% coverage.
- The Alliance must complement polio eradication; strengthening infrastructure and increasing access to routine immunization and improving AFP surveillance is critical in polio-endemic countries.
- Reducing mortality from measles by reaching every child with measles vaccine is a high priority.
- The Alliance should look into the issue of technology transfer of vaccine production and safe injection materials in a pragmatic way. The different aspects (including advantages and disadvantages) of transfer of technology should be analysed and discussed in the GAVI Board in the context of access as well as research and development (R&D).
- NGOs are important stakeholders and partners of the Alliance.
- A comprehensive health perspective must be used when assessing countries' investments in health.
- Sub-account 2 of the Global Fund for Children's Vaccines (GFCV) is an important financing mechanism of the Fund.

- The managerial and financial responsibility for sub-account 2 would be carried out on a country by country basis by the international agency best equipped to do an effective job.
- The Board revised and adopted the broad principles of the document "Immunize Every Child" (Annex 2) and decided it should be distributed widely for consultation before being finalized at the June meeting.

5) An update on the Global Fund for Children's Vaccines (GFCV) (Annex 3) was presented by Dr Mark Kane. The Board:

- decided there would only be one fund and in this context endorsed the principle of the US charity and the Working Capital Account at UNICEF as two components of a single fund;
- welcomed the principle of consultation in the appointment of Board Members of the Fund as well as its Executive Director; proposed interim appointments were endorsed;
- commended the rapid developments towards the Fund's establishment and the initial contribution made of 175 million USD by the Bill and Melinda Gates Foundation;
- requested that an "aide memoire" be prepared for resource mobilisation purposes to clarify the different mechanisms that contributors can use to support GAVI objectives.

6) The Board was informed by Dr Chris Lovelace that work towards establishing an IDA revolving account at the World Bank to strengthen immunization services and the vaccine market is in an advanced stage of development.

7) The Board received an update on R&D-related activities, including incentives for the private sector, and looked forward to discussing this theme in depth at the next Board meeting (Annex 4).

8) The Board requested that for the next Board meeting, the Secretariat and the Working Group outline clear roles and responsibilities relating to the Board's strategic and operational functions.

9) Several Board members expressed the desire to become more involved in the activities of the Alliance and a closer link to the Working Group. The Board also decided to hold at least two teleconferences before the next Board meeting.

10) The Board approved revised job descriptions (Annex 7) and authorized the Executive Secretary to proceed with recruitment.

11) The Board looks forward to the next Board meeting, which had been decided in the October 1999 meeting to take place 13–14 June 2000 in the Geneva area for two full days to discuss Alliance matters in depth.

12) The Board acknowledged the excellent presentations made by Mr Michel Zaffran, Dr Mark Kane, Dr Mike Levine and Ms Amie Batson.

Adopted agenda

1) Introduction by Chair
2) Progress and Challenges: A GAVI brief
3) GAVI Strategy for Sustainable Immunization Services (M. Zaffran)
4) Updates on:
   - The Fund (M. Kane)
   - Research and Development Pre-Task Force (M. Levine)
   - Incentives for R&D: An Overview (A. Batson)
5) Secretariat Positions, Job Descriptions (T. Godal)

List of annexes

Annex 1:
Progress and challenges: a GAVI brief

Tore Godal, Executive Secretary

I have been asked to give this operational statement from the non-operational Secretariat.

Progress

Since the establishment of the Alliance six months ago, in July of the last millennium, substantial progress has been made, including:

- the establishment of a founding Board, an operative Working Group, a Secretariat, and three task forces;
- a Global Fund for Children's Vaccines with a contribution of 175 million USD received in 1999 from the Bill and Melinda Gates Foundation;
- the adoption of the basic principles for use of the Fund's resources at the first Board meeting in October 1999;
- extensive efforts by each partner agency to inform their constituencies about the Alliance through their boards, annual meetings and country visits.

During the last six months we have witnessed a lot of excitement and enthusiasm. We have moved and worked quickly. Unfortunately, this has meant that we have not always been successful in keeping everybody informed and in having everybody participating in every event. This is always frustrating for those left out. It may happen again, but we will try hard to do better.

Challenges

- That the basic principles and strategies to address the five strategic objectives of the Alliance will have been adopted, through discussions taking place at this board meeting and the next, by June 2000.
- That we move towards 'making a difference on the ground'. This is where our energies need to be focused. We should strive for simplicity, be prepared to learn and adapt our procedures and approaches as we move along. We should adopt an experimental attitude as we work with our national partners, recognizing that we do not have all the answers from either a technical or administrative point of view.
- That we strive to fill the gaps in financing by ensuring that the Fund becomes truly international and, importantly, that financial resources through other channels become strengthened.
- That we further strengthen the links to our constituencies. We are exploring

the possibility of holding an Alliance meeting with broad participation of the global immunization community toward the end of this year.

- At the same time we need to complete the establishment of the Alliance with rules for Board and working group participation etc. We hope to do this by the next Board meeting in June.

I was involved in a similar inter-agency development in the 1970s: the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR). I believe this Alliance has progressed as far in six months as TDR did in four years.

This is not only due to progress in communication technologies, but very much due to strong partner commitment, a devoted working group, and a determined Board.

It has been great pleasure for me to become drawn out of retirement to participate in this unprecedented endeavour.

Annex 2:
Immunize Every Child:
GAVI strategy for sustainable immunization services

Advanced draft: February 2000

Table of contents

Executive summary

Nearly 30 million of the 130 million children born every year are not receiving basic immunization. The great majority of unreached children, or 28 million, live in developing countries, and of those 25 million are in the poorest countries, defined as countries that have less than 1 000 USD per capita GNP.

A major priority for the Global Alliance for Vaccines and Immunization is to see that all countries of the world achieve at least 80% immunization coverage by 2005. To achieve that milestone, immunization services must expand to reach 11.3 million more children in the poorest countries.

This discussion paper outlines a strategy for increasing immunization coverage to reach these children. It was reviewed and its main principles were approved by the Board of GAVI at its meeting on 31 January 2000 in Davos, Switzerland. It is now being sent out to a large number of concerned organizations, institutions and individuals for further comments. After that it will be presented to the GAVI Board at its June 2000 meeting for final approval.

The paper is organized into three main sections. The first part proposes general policy directions for the Alliance to achieve its first objective "to improve access to sustainable immunization services". The strategy framework highlights immunization as an essential component in international development efforts; as a global public good; its relation to health sector development; and its connection with the polio eradication effort. Issues to be considered in relation to delivery, access and monitoring of immunization services are also discussed.

The second part of the document describes the operations of the Alliance that will basically be carried out by the partners: governments, UNICEF, World Bank Group, WHO, foundations, industry, public health institutions, and NGOs. Their respective efforts are outlined. The essential roles of the GAVI partners include:

- fundraising;
- working with national governments to increase support;
- advocating increased commitment and allocations to immunization;
- working with new partners to increase their efforts in delivery and outreach.

The third part of the document deals with the principles of financing strategies to improve access to sustainable immunization services. It also presents the general principles and priorities for the use of sub-account 2 (immunization services) of the Global Fund for Children's Vaccines (GFVC, or the Fund).

Based on current assumptions of vaccine delivery costs it is estimated that an additional 226 million USD annually is needed to reach at least 80% coverage in the poorest countries with the traditional EPI vaccines. To cover the same number of children with the newer vaccines, according to the guidelines adopted at GAVI's first Board meeting, would require an additional 352 million USD.

It is likely that most of the funding for immunization services will have to continue to come from national budgets and traditional external sources (bilateral and multilateral funding).

Sub-account 2 of the Fund might attract additional funding for this purpose. The mechanism for access to sub-account 2 is proposed to be the same as that for sub-account 1: country funding proposals based on national immunization plans that are endorsed by the national Inter-agency Coordinating Committee, or comparable group.

Introduction

The mission of the Global Alliance for Vaccines and Immunization is "to save children's lives and protect people's health through the widespread use of vaccines". To achieve this mission, three widening gaps need to be addressed:

- the children who are still not receiving the 'basic six' immunizations as compared to those who are reached through the polio eradication initiative (Table 1);
- the growing disparity in the number of vaccines available to children in industrialized and developing countries (Fig 1);
- the lack of investment in vaccine research and development for diseases that are prevalent in poorer countries.

At its first board meeting, GAVI adopted basic principles on the use of the Global Fund for Children's Vaccines which will contribute to filling the second gap – providing newer vaccines to children living in the poorest countries of the world (Report of the First Board Meeting, GAVI/99.02). A strategy for closing the third gap is under development and is expected to be considered by the GAVI Board at its third meeting in June 2000. The aim of this document is to outline GAVI's strategy to start addressing the first gap.

Since 1990, a declining proportion of the approximately 130 million children born every year becomes fully immunized with the original six EPI vaccines (measles, polio, tuberculosis, diphteria, pertussis, tetanus). While in the early 90s, four out of five children were fully immunized, in 1998 only three out of four children were reported to receive full immunization (see Figure 2). In addition, newer vaccines, such as those for hepatitis B, *Haemophilus influenzae* type b (Hib), and yellow fever have existed for years but are not widely incorporated into immunization programmes in much of the developing world. Thus over 30 million children born every year will not be adequately protected against vaccine-preventable diseases. Of those, 25 million live in countries with less than 1000 USD per capita GNP (see Table 2).

This immunization gap represents a devastating toll on the world's population. Every year, there are three million unnecessary premature deaths, because too many children have not been given the vaccine that could have saved their lives (see Table 3). This is not only a health issue; it is an issue of fundamental equity and human rights.

The challenge facing us is how to expand immunization services to these unreached

children, to recognize the obstacles that countries now face and identify creative strategies for overcoming those obstacles. From the Polio Eradication Initiative (PEI), we have seen countries as large as India give nearly every child under five a vaccine during National Immunization Days (NIDs). Recognizing that other vaccines are not as simple to administer as the oral polio vaccine, there are still important lessons to learn from the success of the PEI.

I. Overall policy directions

Strategy framework

The case for immunization in international development and poverty reduction

The shift in international policy now taking place from economic development to poverty reduction has important implications for immunization. The case for health as a key element of poverty reduction is gaining ground (G7 Köln Summit, London "World Health Opportunity" meeting report). In addition, there have been increasing calls for debt relief for the poorest countries, with the idea of channelling those savings into national health and social programmes. These directions imply giving priority to combating conditions that are causing excess disease burden in poor populations. In this context the case for immunization is:

- Infectious diseases are among those diseases showing the highest differentials between poor and non-poor;
- Vaccine-preventable diseases account for over 20% of that "excess" burden (Table 4);
- Immunization is among the most cost-effective interventions (Table 5); and
- Among health interventions, immunization has demonstrated high potential for reaching the poorest populations even in the absence of other aspects of health services.

Since it can be monitored more easily than most other services, immunization lends itself as an important outcome measurement to highlight progress in global poverty reduction.

Policy direction:

Immunization services should be given a high priority in poverty reduction efforts.

Immunization as a global public good

Immunization leads to reduced transmission of diseases within and between countries. As travel and contacts across borders increase, immunization in one country tends to become more important in the reduction of transmission to other countries.

Thus immunization has impact that reaches far beyond the individuals immunized.

In addition, immunization can lead to disease eradication. Eradication of a disease, as was the case with smallpox and will soon be a reality for poliomyelitis, can be considered an ultimate example of global public good. While the total cost of eradication of smallpox has been estimated to 300 million USD the annual savings amounted to some 250 million USD, in addition to the reduction of extensive human suffering. Likewise polio eradication, which may cost the global community 1.8 billion USD over almost 20 years, will save 1.5 billion USD annually in averted treatment and immunization costs.

Policy direction:

Immunization must be maintained as a global public good since it benefits every community, country and region of the world.

Immunization in Health Sector Development

Immunization is provided through facilities, staff and operations dedicated to public or private health services. Thus, the overall performance of the health sector has a strong influence on the quality and coverage of immunization services. Conversely, appropriately planned immunization services can also contribute to the overall development of the health sector. Traditionally this relationship has been viewed as contentious, either a "horizontal" or "vertical" issue.

Analyses of health sector reforms undertaken during the 1990s show that this does not need to be the case.[1] In fact, profound reforms including sector-wide approaches can contribute to higher immunization coverage levels (S. Adjei 99). Moreover, a recent review of the impact of polio eradication on health systems shows that synergies can be achieved, provided that the eradication efforts are adequately planned (Stenson & Mogedal 99).

Any increased investments in the health sector, as part of a poverty reduction strategy, must address the need for health services to reach out to populations in remote areas. This outreach should strengthen opportunities for synergies in the delivery of basic health care to poor populations, such as combining immunization with nutrition and family planning programmes.

Thus, health sector reforms need to improve people's health by responding to legitimate needs. As a public good, immunization requires strong public policies and finance. However, the delivery of services is increasingly segmented into different kinds of public and private sectors (World Development Report 1993, HNP white paper 1997). This increased complexity requires increased central and peripheral managerial capacity, and increased emphasis on outcomes rather then specific inputs (Washington meeting).

[1] Health sector reform and priority health interventions: The case of immunization services. Washington, 1999-11-15-16

There is also a need to further analyse the cost of immunization programmes in relation to broader health-related investments.

Policy directions:

Strengthen immunization services to synergize within overall health sector plans and development.

Shift emphasis pragmatically, as health systems development permit, from specific inputs to specific outcomes.

Respond to urgent need to strengthen national capacity to plan and manage immunization services in the broader context of health sector development.

The Polio Eradication Initiative and GAVI

In 1988, the World Health Assembly resolved to eradicate polio from the world by the year 2000. This goal is within our reach and the Polio Eradication Initiative (PEI) is now among the highest priorities for the global immunization community.

This initiative received some 300 million USD in external support during 1999, in its final phase of operation, according to WHO. Transmission is expected to be interrupted by the end of year 2000 or shortly thereafter. Financing requirements are expected to start to decline by 2001, but in order to reach the goal, continued selective field operations will be needed for several years, at least until 2005, requiring an additional estimated total of 1 billion USD.

The polio eradication initiative is an effective global effort that reaches virtually every child in the world. Political commitment and mobilization of civil society has proven to be instrumental in the initiative's ability to reach the unreached. With contributions to the campaign ranging from heads of state making national radio appeals, to football stars and other celebrities involved in public events, to local volunteers making community appeals, the global momentum achieved is a model for immunization activities.

PEI has developed clear roles and responsibilities for different partners at global, regional and national levels, and managerial and communications mechanisms between all these levels and partners. These represent important opportunities for GAVI that will materialize only if there is close collaboration between GAVI and the Polio Eradication Initiative at all levels.

- At country level: GAVI will build on polio activities in several ways:
    1) Improving access to all vaccines based on lessons learned from NIDs. Feasibility studies are in progress with support from the UN Foundation.
    2) The PEI is a major investor in cold chain equipment and GAVI partners could complement these activities.
    3) During year 2000, staff currently involved in EPI/polio will do broader work for immunization-related activities which will benefit GAVI, such as helping develop five-year plans, contributing to the strategic vision, helping in priority setting and microplanning, etc.

4) In many countries the polio initiative is coordinated through an Inter-agency Coordination Committee (ICC). Its mandate must be broadened to encompass all immunization efforts which can be used for GAVI's objectives.

- At regional level: the EPI/PEI has strong regional teams that provide leadership for field operations – a network upon which GAVI should build. Regional ICC mechanisms, which bring in many partners and address the full immunization agenda, already exist and can be also integrated into GAVI efforts.
- At global level:

1) Global polio partners provide technical assistance (CDC, RIVM, NIBS etc), carry out research (universities etc), provide fundraising, advocacy, in-country volunteers (Rotary etc), financing (donor agencies, World Bank etc), and staff (CDC, US, Canada etc). As country-specific plans are being developed for GAVI-related activities they will be available for partners through the same channels as for polio, and vice versa. The activities will be closely coordinated in order to ensure that competition in resource mobilization is avoided.
2) Advocacy and communication activities will also be coordinated at the global and country levels to ensure synergy and avoid simultaneous media action and conflicting messages.

Policy direction:

Polio eradication is a time-limited initiative. Its external financial requirements will start to decline by 2001. GAVI has broader and longer term goals. The Polio Eradication Initiative and GAVI seek to maximize this complementarity through close collaboration to fulfil their respective missions. This collaboration will be considered on a country-by-country basis, strongly respecting the needs of the final polio eradication efforts. As it has been clearly shown that polio eradication benefits from a strengthening of immunization infrastructure and increased access to routine immunization, GAVI encourages support to these components in all countries, including those taking part in the intensified polio eradication effort.

Immunization Services

Delivery

While vaccinations are remarkably effective and provide longer term protection in comparison to many other health interventions, the delivery of effective services rely on the existence of a number of essential components that require rigorous attention (WHO, doc. in preparation). They include:

- Supply and quality of vaccines (forecasting, procurement, production)
- Logistics support (transport, cold chain, supplies, waste management)
- Communication (advocacy, social mobilization, programme communication)
- Surveillance (routine reporting, case investigation, diagnostics, active surveillance)

- Service delivery (policy and strategy development and guidelines, planning, coordination and budgeting, supervision and monitoring).

GAVI milestones
During 2000, GAVI will present an analysis of current market and policy failures concerning levels of research, development and commercialization of candidate vaccines for HIV/AIDS, malaria and tuberculosis and make recommendations to overcome these problems.
By 2005, 80% of developing countries will have routine immunization coverage of at least 80% in all districts.
By 2002, 80% of countries with adequate delivery system will introduce hepatitis B vaccine and all countries by 2007.
By 2005, 50% of poorest countries with high burden of disease and adequate delivery systems will have introduced Hib vaccine.

Some components require central national attention that can be shared with other similar functions, but not be de-centralized (vaccine procurement, policy development). Others need to be de-centralized in harmony with reforms (staff costs, distribution, etc), while most require both central and peripheral attention to operate effectively. Experience from the Americas has shown that an effective execution of immunization services requires forward planning. GAVI partners recognize how crucial it is for countries and districts to develop multi-year health plans in which immunization is a key priority, and build the adequate capacity for management of immunization services. The importance of good management can hardly be overemphasized and strengthening of the management capacity of countries thus becomes one of GAVI's major challenges.

In the past, governments have functioned as if the financing, management and execution of health services were the sole responsibility of the central health ministries. In recent years, a shift has occurred toward recognizing the role that the *delivery* of health services quite often falls to community organizations, the private sector, and NGOs. With this revision of roles and responsibilities in service delivery, there is new pressure for governments to increase their emphasis in quality control, monitoring, surveillance and assessment. Current critical indicators are set out in Table 6; a common assessment toolbox for use by all GAVI partners is being developed and tested (expected to be available by mid 2000).

With the policy adopted at its first board meeting, GAVI committed itself to take newer vaccines to populations in need. Specifically, hepatitis B vaccine should be introduced into all eligible countries, Hib vaccine into Africa and other countries in which the disease burden has been demonstrated, and yellow fever vaccine in countries at risk. The introduction of the newer vaccines can only been done in countries with reasonably functioning routine immunization services. In particular, it is of high priority for GAVI that the mortality from measles (presently 900 000 children's deaths per year) is brought down by reaching every child with measles vaccine.

In order to reach out to the target population it is important that vaccines be deliverable in a safe, simple and most effective fashion. The simplest way to provide them and to reach out to the target population is by using a combination of four (DTP+Hep B) or five (DTP+Hep B+Hib) vaccines together, administered through a safer technology such as monodose delivery devices. The packaging and formulation of these new vaccines need to fit within the logistic limitations of the low-income countries.

Policy direction:

GAVI recognizes that immunization services can only be effectively delivered if all components are fully operational. That should be assured through a judicious mix of central and de-centralized functions.

The increased number of players involved in service delivery require that the public sector strengthens its function for monitoring, surveillance and assessment and establishes mechanisms for collaboration with private providers.

GAVI promotes the use of new and safe technologies such as vaccine combinations and monodose delivery devices that will facilitate reaching the unreached.

Access

The greatest challenge to fulfill GAVI's mission is to increase access to immunization services for the currently unreached children, especially the 25 million born every year in the low-income countries.

Practical experiences over the last few years have pointed to a variety of mechanisms that can be used to improve access.

Health sector reforms

Reforms can work in both directions with regard to access to immunization services. There is a need for further analysis of the impact of health-sector reforms on immunization coverage. Positive reforms have been found to include:

1) Shifting resources from tertiary to primary care
2) Engaging private-practice health workers in immunization services
3) Protecting and increasing financing of outreach activities, especially for travel and subsistence allowances
4) Making access to immunization a performance indicator in health systems financing.

Community-based action

The importance of communities in health activities has become increasingly apparent:

1) Community-directed distribution of ivermectin has proven superior to health services-based distribution.
2) Communities can facilitate transport and other support functions.
3) Community-created demand through active involvement in disease surveillance such as measles.

Combined community and health services-based action

The most effective approach in reaching the highest coverage is the polio national immunization days, which combine community mobilization with health services outreach. An added important aspect of NIDs is their regular campaign modes (i.e. focused on a certain day). This does not necessarily need to be a national day but could be a regional or district day(s).

Combining various interventions

There may be advantages in combining interventions that can be delivered simultaneously at the most peripheral level. They could include vitamin A supplementation, intermittent administration of drugs (such as ivermectin for river blindness, albendazole for intestinal helmints, drug combinations for lymphatic filariasis), distribution of insecticide-treated mosquito nets, and the kit for their re-impregnation.

Through operational research, each country will identify the most effective means of improving access to the most appropriate combination of interventions. In this operational research attention, should be paid to a possible transfer of relevant technologies and the effectiveness thereof.

Policy directions:

GAVI promotes health-sector reforms that increase sustainable access to vaccinations and other health interventions.

Through advocacy and other mechanisms GAVI will support work that promotes community demand, ownership and action.

GAVI will collaborate with other initiatives like Roll Back Malaria, African Program for Onchocerciasis Control and Micronutrient Initiative to develop effective campaign strategies to reach the most inaccessible populations.

Monitoring and evaluation

The need for monitoring and evaluation extends to the whole of the immunization services as part of the health system. The main role of GAVI is to promote and ensure the introduction of comprehensive and joint monitoring systems in the countries concerned. Harmonization with other reviews and health sector evaluations is essential.

New monitoring and evaluation instruments are now being developed and piloted by the partners. These tools are being expected to be ready for large-scale use during year 2000.

The basis for monitoring and evaluation will be the national multi-year immunization plan into which the monitoring system should form an integral part, and implementation by the ICC. In addition there may be a need for in-depth reviews to be undertaken intermittently as required, most commonly at mid-term and at the end of a five year plan.

All country support from the GFCV will be allocated on the basis of one comprehensive country proposal. Contributions from the GFCV will be included in the comprehensive monitoring system with particular responsibility given to one of the GAVI partners at the national level. This partner will also be responsible for accounting as required. The focus of the evaluations will be on outcomes and achievements.

Policy directions:

GAVI promotes comprehensive, outcome-oriented monitoring and evaluation systems as integral parts of the national multi-year immunization plans.

GAVI will seek joint monitoring action together with all other concerned partners including the national governments.

II. GAVI implementation mechanisms

The main responsibility for immunization services – as an integral and essential part of health sectors – rests with national governments. A major responsibility for supporting countries in the improvement and extention of immunization services lies with those international, multilateral, bilateral and other organizations that are active in international development cooperation in health.

GAVI does not change that. As an international alliance of operational partners, the GAVI Board, working group and task forces will work to identify overall needs to strengthen immunization, and encourage members of the Alliance to increase their activities in order to fill the gaps. GAVI partners will strive to work through existing regional and national Inter-agency Coordination Committees (ICC), to identify needs and plan activities.

The role of GAVI is therefore to strengthen the explicit and complementary roles of each individual partner in the Alliance, as they are described below.

Governments of low-income and middle-income countries

Primary

To ascertain that the health sector develops effective measures to reach out and provide health services to those most in need.

Supportive

- To assure that health in general and immunization in particular receive a justified and identifiable proportion of the government budget.
- To coordinate external inputs to immunization, develop, monitor and evaluate multi-year immunization plans.
- To collaborate with communities and private providers.

Governments of high-income countries

Primary

To ensure that health gets an adequate proportion of external aid channelled through the sector coordination mechanisms.

Supportive

- To ascertain that pro-poor global policies are made and implemented.
- To ensure that health is given adequate priority in the context of poverty reduction as well as a global public good.
- To facilitate the prioritization of immunization in national health institutions and participation in international efforts.
- To support the strengthening of immunization services through broad sectoral approaches.

UNICEF

Primary

To advocate and mobilize leaders from global to community levels to set immunization of children as a key priority for development.

- To provide mechanisms for procurement of vaccines and equipment.
- To facilitate functioning of mechanisms for national coordination of immunization services.

Supportive

- To provide technical and logistics support for expansion of outreach services,
- To provide technical and financial support to enhance community action for access to immunization services.

World Bank Group

Primary

Within a broader perspective of poverty reduction and economic development to take primary responsibility with national governments to work toward sustainable financing mechanisms in the longer term for immunization services including vaccine purchase and infrastructure support.

Supportive

- To enhance more effective involvement of Departments of Finance, Economics and others to become full partners in reaching full immunization coverage,
- To support and carry out analyses relating to the economics of immunization.

World Health Organization

Primary

Developing global policies and strategies for immunization and vaccine development and advocacy for these.

Supportive

- Providing technical and financial support to governments to strengthen the health sector capacity to improve access to immunization services and surveillance systems;
- Facilitating the functioning of mechanisms for national coordination of immunization services;
- Providing national and regional capacity networks to promote technical efficiency and capacity through the development of common policy frameworks;
- Providing support for disease-burden studies and effectiveness trials to assess the importance of newer vaccines at the country level.

Foundations

With their flexibility and rapid response potential, Foundations will:

- Provide financial support to the Global Fund for Children's Vaccines,
- Mobilize new resources for the Fund,
- Provide support to lead agencies in support of analytical, policy and operational work, and
- Support catalytic action at country level.

Pharmaceutical industry

The developers and producers of vaccines and immunization supplies will:

- Contribute actively to supply high quality vaccines to the poorest population,
- Contribute actively to the development and supply of new breakthrough vaccines on a worldwide basis,
- Develop technologies to facilitate the distribution and administration of vaccines within countries,
- Contribute to the education of immunization providers in these countries,
- Engage every private sector in the mission of GAVI.

Public health institutions

In relation to access and infrastructure, these institutions (eg MOH public health institutions like CDC, NIH, NIBS, State Serum Institute etc.) will:

- Facilitate setting global policies,
- Work as reference laboratories for surveillance and quality control, and
- Provide technical staff for operations and capacity building.

Non-governmental organizations (e.g. Rotary International)

As part of the civil society and in view of its growing role, NGOs are expected to:

- Support immunization in countries as part of their health programmes,
- Advocate the need to strengthen immunization and health systems, and
- Contribute to fundraising for immunization in various forms.

III. Financing the gaps

Assumptions

There are limited data available for the costs of immunization services in various countries and development assistance resource flows for immunization (except for polio eradication), making it difficult to calculate global costs and financial gaps.

Therefore, the calculations below are based on average standard costs for immunization services as defined through previous studies[2], and knowledge of vaccine prices (based on current prices). As the costs range considerably between countries, these calculations cannot be applied to individual countries without making further assumptions about their specific cost structure. However, we anticipate that more precise data can be derived from the forthcoming country proposals, country by country, to be compiled on a regional and global basis.

It is assumed that the expansion of services will necessarily incorporate a share of the capital and indirect costs, also based on the fact that we do not know the breaking points between fixed and variable costs.

The most important cost elements required to increase access are recognized to be:

- Management and operations
  - training and capacity strengthening
  - salaries and allowances
  - monitoring and evaluation
  - operational research for innovation
  - communication, social mobilization and community participation
- Supplies and maintenance
  - vaccines and safe injection materials
  - fuel
  - spare parts and services
- Capital investments: equipment for
  - cold chain
  - telecommunications
  - computing

[2] Brenzel and Claquin, 1994; WHO-V&B, Cost estimates of expanding immunization services in selected HIPC countries, 1999

The birth cohort is projected to be roughly constant over the next ten years. This does not necessarily hold true for individual countries although it is correct for the group of countries "less developed regions" (1998 revision of the United Nations World Population Estimates and Projections). This year's birth cohort in the countries with below 1,000 USD per capita GNP is 91 million. Of these, 66 million are being immunized through routine immunization programmes. Thus, 25 million children remain unimmunized. To achieve at least 80% coverage in all countries, 11.3 million of these children have to be reached (see Table 7).

The cost of fully immunizing a child with the six traditional EPI vaccines through routine health services were estimated to be approximately 15 USD per child in the 1980s and approximately 17 USD per child in the 1990s. Thus, with an annual birth cohort of approximately 91.4 million in low-income countries, estimates of total immunization costs in 1998 were 1.123 billion USD.

To reach inaccessible populations costs more than static services with a progressive increase in the marginal cost for every new child as coverage approaches 100%. Outreach services have been estimated to cost on average 26 USD per fully immunized child, with a range of 16 USD to 48 USD. Thus the marginal cost to immunize children up to a coverage of 80% has been calculated to increase by 3 USD (i.e. from 17 to 20 USD per child) and by 8 USD (i.e. from 17 to 25 USD per child) above 80% coverage.

Financial requirements

Out of the annual birth cohort in the developing countries of 117.7 million, 28.0 million children are currently unreached by immunization. Of these 25.3 million live in the low-income countries.[3]

The cost of immunization for *all* developing countries is shown in Fig. 1. The current investment in immunization in these countries is 1.564 billion USD annually. To reach 80% coverage with the traditional and newer vaccines would require 2.310 billion USD and to reach all children would require a total of 2.808 billion USD.

The cost of immunization for the *low-income* countries only is shown in Fig. 2. The current investment in immunization in these countries is 1.133 billion USD annually. To reach 80% coverage with the traditional and newer vaccines would require a total of 1.711 billion USD and to reach all children would require a total of 2.132 billion USD.

The cost of adding the new vaccines against hepatitis B, *Haemophilus influenzae* type b, and yellow fever (vaccine cost of 1 USD per child for administration) has been calculated according to the country-specific patterns of disease burden.[4] For further information see Table 8.

[3] Low-income countries are defined as those with a GNP/capita below 1000 USD, middle-income countries with a GNP/capita between 1000 USD and 9360 USD. The notion of developing countries is used for these two categories together.

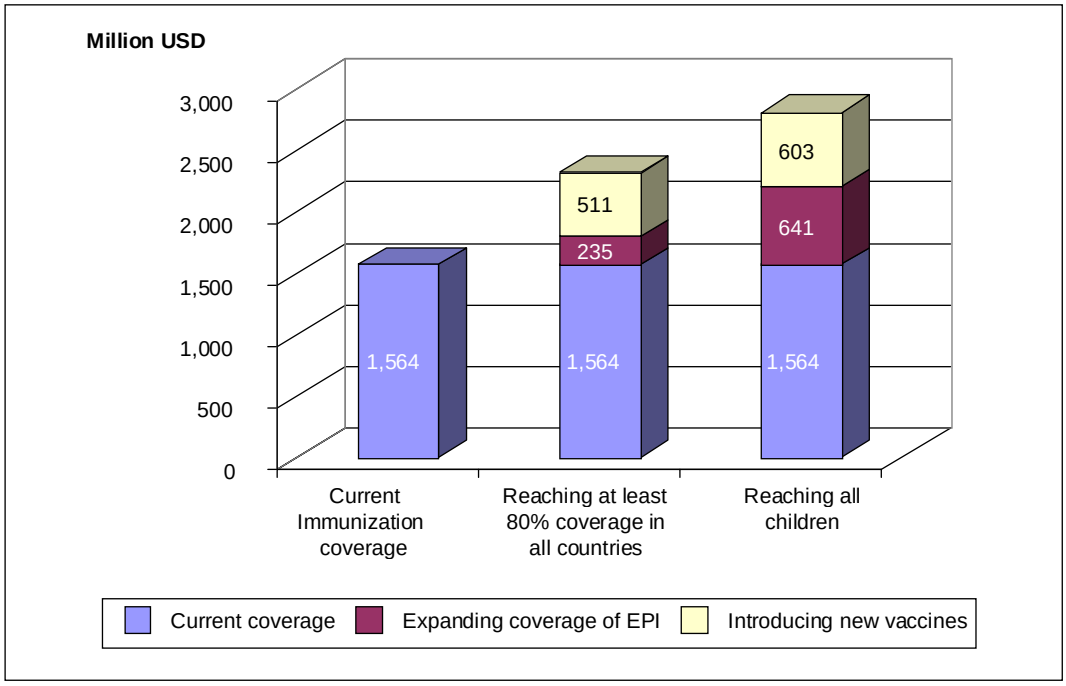
[4] These amounts are based on existing policy for which Hib vaccine is not introduced in Asian countries, and the Yellow Fever vaccine is introduced only in endemic countries.

In summary about 95% of the costs for expanding access to the traditional vaccines would fall on the low-income countries. For the introduction of the newer vaccines about three quarters of the costs would be required for the low-income countries.

If the national governments of low-income countries continue to bear at least the costs of fixed facilities and staff of immunization services (estimated to be some 50% of total costs), external assistance requirements to increase access to the traditional vaccines will be roughly half of these figures. Achieving coverage goals with the new vaccines will require a greater proportion of external assistance.

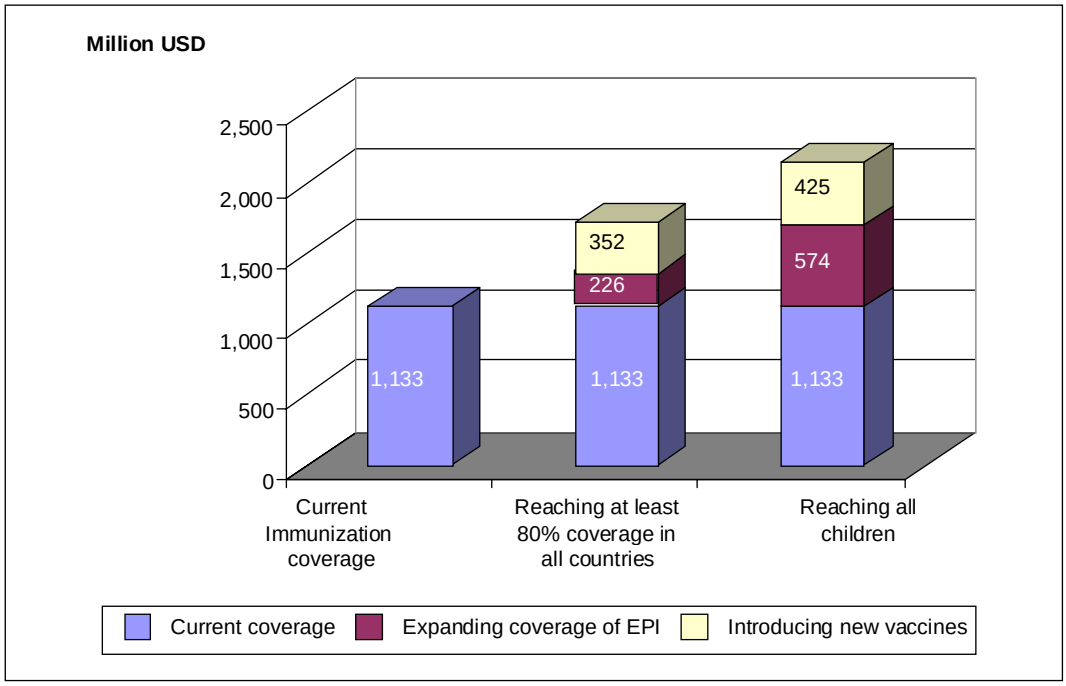
In addition to the requirement to finance an extension of the coverage with the traditional vaccines and the introduction of the new vaccines the polio eradication initiative will continue to require funding to the tune of 1 billion USD (out of which some 700 million USD have already been committed) over the next six years.

Figure 1: Cost for increasing immunization in low and middle income countries



The costs of introducing new vaccines in middle income countries may represent an over-estimate, because of under-reported introductions.

Figure 2: Cost for increasing immunization in low income countries only



The role of GAVI partners in closing the gaps

National governments bear the main financial burden of health and immunization services in their respective countries. The responsibility for ensuring an expansion of current services to underserved groups, and including the new vaccines in their immunization schedules, will continue to fall mainly on governments. Many countries have demonstrated that substantial parts of infrastructure expansion can be met through their own budgets and through sector wide financing; this is the preferred mode of financing. In addition, strategies (including operational research) to reduce wastage and contain costs should be a natural part of the national immunization plan. Thereby a more cost-effective delivery of immunization services will be achieved.

Even so, in many instances there appears not to be sufficient resources currently to meet the cost of expansion of immunization services that has been outlined above; in early discussions with countries, a number of them have indicated a need for external support for infrastructure development. This external support should be sought primarily from increases in bilateral assistance to countries, new loans from the World Bank and regional development banks, and increases in funding from multilaterals (mainly UNICEF and WHO). GAVI Secretariat and partners therefore will work to encourage and assist in:

- fundraising by coordinated appeals;
- supporting national governments in loan requests;
- advocating for increased allocation of international development funds for immunization;
- working with governments to ensure that immunization is among the highest priorities of the national health system and that it receives appropriate internal resources;
- working with NGOs and community organizations to increase funding for health service delivery and outreach efforts.

The national ICCs will play a crucial role in providing an opportunity for the partners to consider support to specific items and in the co-ordination of external financial assistance.

Global Fund for Children's Vaccines

The Global Fund for Children's Vaccines is a new experiment in the international public health community. The Fund has three sub-accounts (or windows) for disbursements: 1) vaccines and safe injections materials; 2) vaccine access and infrastructure; and 3) vaccine research and development.

The Bill and Melinda Gates Foundation has provided the first contribution to the Fund through a commitment of 750 million USD over five years. This contribution is primarily targeted for sub-account 1 – the procurement of new vaccines (see GAVI Report of First Board Meeting, 1999). This contribution will provide approximately 40% of the resources required to cover the target population > 80% with the newer vaccines (Table 2).

Should contributors and recipient countries wish resources to be channelled to sub-account 2, these funds will be used to fill resource gaps not covered by other partners for strengthening access and infrastructure in low-income countries (<1000 USD per capita GNP) to increase their immunization coverage. The proposed general priorities for funding from sub-account 2 are:

- to help countries meet the assessment criteria required to receive support for procurement of newer vaccines under sub-account 1 of the Fund;
- to facilitate multi-partner collaboration;
- to fund cost elements critical to increase access.

The basic mechanisms for providing financial support from sub-account 2 of the Fund will be the same as for sub-account 1:

- country funding proposals submitted to GAVI need to be based on a multi-year plan including strategies to achieve increased immunization coverage;
- the country plan needs to be endorsed by the national Inter-agency Coordination Committee and be explicit about contributions from partners.

In using sub-account 2 resources, concerns that have been raised about monitoring mechanisms, the risk of substitution of other funds and raising unrealistic expectations will be taken into consideration.

The following procedures for applications to the Fund are foreseen:

- that country proposals will first be reviewed by ICCs;
- that ICC partners will consider how they can contribute to meet the financial gaps of the plans;
- that only unmet needs will be forwarded to GAVI to be considered for financing from the Fund.

Appendix:

Tables and figures

Table 1: Comparison of Polio3 routine coverage and Polio NID coverage

Country	1997 Coverage with third polio dose in routine services	Highest coverage achieved during polio NIDs	Percent new-borns remaining without a single contact with routine EPI services
Angola	38	90	**32**
Cameroon	47	103	**47**
Chad	24	108	**55**
Comoros	48	na	**45**
Congo	21	91	**71**
Dem. Rep. of Congo	18	95	**na**
Kenya	36	82	**58**
Mauritania	28	95	**71**
Niger	28	103	**66**
Nigeria	45	95	**47**
Sierra Leone	26	na	**62**
Togo	33	104	**47**

Source: World Health Organization

Table 2a: The "unreached" children in low-income countries

	Country	GNP per capita	Public health budget as % of GDP	Birth cohort (in 2000)	DTP3 coverage	Unreached children	
#		(USD)	(Percent)	(Thousand)	(Percent)	(Percent)	(Thousand)
1	**Afghanistan**	n.a.	n.a.	1157	34	66	764
2	**Albania**	810	2.5	60	96	4	2
3	**Angola**	340	3.3	607	36	64	388
4	**Armenia**	480	3.1	47	82	18	8
5	**Azerbaijan**	490	1.1	121	97	3	4
6	**Bangladesh**	350	1.2	3 524	78	22	775
7	**Benin**	380	1.7	247	81	19	47
8	**Bhutan**	n.a.	2.3	77	86	14	11
9	**Bolivia**	1000	4.1	266	76	24	64
10	**Bosnia & Herzegov**	n. a.	n.a.	41	89	11	5
11	**Burkina Faso**	240	2.3	541	*70	30	162
12	**Burundi**	140	0.8	276	50	50	138
13	**Cambodia**	280	0.7	355	64	36	128
14	**Cameroon**	610	1	583	48	52	303
15	**Central Afr Rep**	300	1.9	134	45	55	74
16	**Chad**	230	3.7	329	23	77	253
17	**China**	750	2.1	19 497	98	2	390
18	**Comoros**	370	0.9	25	75	25	6
19	**Congo, Dem Rep**	110	0.2	2 316	18	82	1 899
20	**Congo, Rep**	690	3.2	125	*23	77	96
21	**Côte d'Ivoire**	700	1.4	546	64	36	197
22	**Cuba**	n.a	7.9	137	99	1	1
23	**Djibouti**	n. a.	n.a.	23	*62	38	9
24	**Eritrea**	200	1	150	60	40	60
25	**Ethiopia**	100	2	2 746	57	43	1 181
26	**Gambia**	340	2	51	96	4	2
27	**Georgia**	930	0.6	68	86	14	10
28	**Ghana**	390	1.4	736	68	32	236
29	**Guinea**	540	1	313	56	44	138
30	**Guinea-Bissau**	160	1.1	50	*63	37	19
31	**Guyana**	770	4.3	17	90	10	2
32	**Haiti**	410	1.3	257	22	78	200
33	**Honduras**	730	2.8	206	96	4	8
34	**India**	430	1.2	24 316	73	27	6565
35	**Indonesia**	680	0.6	4 539	65	35	1589
36	**Kenya**	330	1.6	994	64	36	358
37	**Korea, DPR**	970	n.a.	456	37	63	287
38	**Kyrgyz Republic**	350	3.5	114	97	3	3

(*) reported coverage prior to 1998

Table 2a (*Continued*)

	Country	GNP per capita	Public health budget as % of GDP	Birth cohort (in 2000)	DTP3 coverage	Unreached children	
#		(USD)	(Percent)	(Thousand)	(Percent)	(Percent)	(Thousand)
39	**Lao PDR**	330	1.3	207	55	45	93
40	**Lesotho**	570	4.1	74	*57	43	32
41	**Liberia**	n. a.	n.a.	142	19	81	115
42	**Madagascar**	260	1.1	608	68	32	195
43	**Malawi**	200	2.3	505	96	4	20
44	**Mali**	250	1.2	515	53	47	242
45	**Mauritania**	410	1.1	106	*28	72	76
46	**Moldova**	410	4.9	56	97	3	2
47	**Mongolia**	400	4.4	58	94	6	3
48	**Mozambique**	210	4.6	832	77	23	191
49	**Myanmar**	n.a.	0.4	938	87	13	122
50	**Nepal**	210	1.2	793	76	24	190
51	**Nicaragua**	390	5.3	176	86	14	25
52	**Niger**	190	1.6	506	25	75	380
53	**Nigeria**	300	0.3	4239	21	79	3349
54	**Pakistan**	480	0.8	5390	79	21	1132
55	**Papua New Guinea**	890	2.8	150	58	42	63
56	**Rwanda**	230	1.9	309	*77	23	71
57	**São Thomé**	280	6.2	6	73	27	2
58	**Senegal**	530	2.5	370	65	35	130
59	**Sierra Leone**	140	1.5	218	56	44	96
60	**Solomon Islands**	750	4.8	15	69	31	5
61	**Somalia**	n. a.	n.a.	517	24	76	393
62	**Sri Lanka**	810	1.4	329	94	6	20
63	**Sudan**	290	n.a.	955	72	28	267
64	**Tajikistan**	350	5.8	187	94	6	11
65	**Tanzania**	210	2.5	1347	74	26	350
66	**Togo**	330	1.2	188	36	64	120
67	**Turkmenistan**	n.a.	1.2	120	99	1	1
68	**Ukraine**	850	5	482	98	2	10
69	**Uganda**	320	1.8	1107	46	54	598
70	**Uzbekistan**	870	3.5	653	99	1	7
71	**Vietnam**	330	1.1	1638	94	6	98
72	**Yemen**	300	1.1	831	68	32	266
73	**Zambia**	330	2.6	382	*70	30	115
74	**Zimbabwe**	610	2.2	355	70	30	107
	Total			**91 351**			**25 276**

(*) reported coverage prior to 1998

Table 2b: The "unreached" children of the middle-income countries*

	Country	GNP per capita 1997	Public health budget as % of GDP	Birth cohort (in 2000)	1998 DTP	Unreached children	
#		(USD)	(Percent)	(Thousand)	(Percent)	(Percent)	(Thousand)
1	**Algeria**	1490	3.3	885	80	20	177
2	**Argentina**	8570	4.3	721	83	17	123
3	**Bahrain**	7820	....	11	98	2	0
4	**Barbados**	6590	4.4	3	93	7	0
5	**Belarus**	2150	5.3	101	97	3	3
6	**Belize**	2740	6.0	7	87	13	1
7	**Botswana**	3260	1.6	53	82	18	10
8	**Brazil**	4720	1.8	3350	94	6	201
9	**Bulgaria**	1140	5.5	71	96	4	3
10	**Cape Verde**	1090	3.4	13	80	20	3
11	**Chile**	5020	2.5	288	92	8	23
12	**Colombia**	2280	2.9	987	70	30	296
13	**Costa Rica**	2640	6.3	91	85	15	14
14	**Croatia**	4610	8.5	47	93	7	3
15	**Czech Rep**	5200	7.4	89	98	2	2
16	**Dominican Rep**	1670	1.8	194	74	26	50
17	**Ecuador**	1590	2.0	309	85	15	46
18	**Egypt**	1180	1.6	1712	96	4	68
19	**El Salvador**	1810	2.4	167	99	1	2
20	**Equatorial Guinea**	1050	5.2	18	*81	19	3
21	**Estonia**	3330	6.4	12	94	6	1
22	**Fiji**	2470	2.3	18	86	14	3
23	**Gabon**	4230	0.5	44	*54	46	20
24	**Guatemala**	1500	1.7	404	89	11	44
25	**Hungary**	4430	6.8	95	100	0	0
26	**Iran**	1780	2.8	1414	100	0	0
27	**Jamaica**	1560	2.5	54	85	15	8
28	**Jordan**	1570	3.7	227	91	9	20
29	**Kazakhstan**	1340	2.2	286	98	2	6
30	**Latvia**	2430	4.4	20	94	6	1
31	**Lebanon**	3350	2.1	71	96	4	3
32	**Lithuania**	2230	4.8	36	93	7	3
33	**Lybian Arab Jam.**	5540	....	162	97	3	5
34	**Malaysia**	4680	1.5	515	95	5	26
35	**Maldives**	1150	4.9	10	97	3	0
36	**Malta**	8630	....	5	92	8	0
37	**Mauritius**	3800	2.3	18	90	10	2
38	**Mexico**	3680	2.4	2310	96	4	92
39	**Micronesia**	1980	....	19	80	20	4
40	**Morocco**	1250	1.6	694	93	7	49

Table 2b (*Continued*)

	Country	GNP per capita 1997	Public health budget as % of GDP	Birth cohort (in 2000)	1998 DTP	Unreached children	
#		(USD)	(Percent)	(Thousand)	(Percent)	(Percent)	(Thousand)
41	**Namibia**	2220	3.7	60	74	26	16
42	**Oman**	4950	2.5	90	100	0	0
43	**Panama**	3080	4.7	61	98	2	1
44	**Paraguay**	2010	1.8	167	84	16	27
45	**Peru**	2460	2.2	608	98	2	12
46	**Philippines**	1220	1.3	2062	87	13	268
47	**Poland**	3590	5.0	420	*95	5	21
48	**Romania**	1420	3.6	201	*97	3	6
49	**Russian Feder.**	2740	4.1	1455	97	3	44
50	**Samoa**	1150	3.1	5	100	0	0
51	**Saudi Arabia**	6790	….	713	94	6	43
52	**Slovakia**	3700	4.6	58	99	1	1
53	**South Africa**	3400	3.6	1051	*73	27	284
54	**Suriname**	1240	2.0	8	90	10	1
55	**Swaziland**	1440	2.8	37	76	24	9
56	**Syrian Arab Rep.**	1150	….	481	97	3	14
57	**TFYR Macedonia**	1090	7.3	32	97	3	1
58	**Thailand**	2800	1.4	993	*95	5	50
59	**Trinidad & Tobago**	4230	2.1	18	91	9	2
60	**Tunisia**	2090	3.0	192	96	4	8
61	**Turkey**	3130	2.7	1396	79	21	293
62	**Uruguay**	6020	7.0	58	87	13	8
63	**Vanuatu**	1310	3.3	6	*93	7	0
64	**Venezuela**	3450	3.0	575	39	61	351
	Total			**26 278**			**2772**

* GNP/capita 1000–9360 USD

Table 3: Mortality from vaccine-preventable diseases

Disease	Estimated Annual Deaths
Polio	720
Diphtheria	5 000
Pertussis (whooping cough)	346 000
Measles	888 000
Tetanus (including 215 000 neonatal tetanus)	410 000
Haemophilus influenzae b (Hib)	400 000
Hepatitis B	900 000
Yellow Fever	30 000
Total	**2 979 720**

Source: The World Health Report, 1999

Table 4: Annual global mortality from diseases that disproportionately affect the poor

Disease	Estimated annual deaths in millions
TB	1.5
HIV/AIDS	2.6
Maternal	0.5
Malaria	1.1
Diarrhea	2.2
Respiratory Infections (-Hib)	3.1
Vaccine Preventable (+Hib, HepB)	3.0
Total	**14.0**

Source: The World Health Report 1999; AIDS epidemic update: December 1999

Table 5: Cost-effectiveness of immunization vs. select other interventions

Intervention	Cost per DALY/life-year gained in USD	Cost per death averted in USD	Comments and sources
Measles immunization (2–15)	<11.7	351 1993	Foster, *et al* in Jamison
Tetanus immunization Campaigns Routine	2.3 ® 11.7	115 (52 –2 750) 89 (27 –205)	Steinglass, *et al* in Jamison 1993
OPV	23 – 49	784 –1 872 Jamison 1993	Jamison, *et al* in
BCG	8.2		In high infection risk environment
EPI+ Cluster of interventions (micronutrients & Hep B) In low-income countries	14–20		Jamison 1994
Meningococcal Meningitis 1 dose, Africa 4 doses, Africa	11–318 24–693	1 125–33 133 2 485–71 660	Miller, Wenger et al 1999
HepB immunization	29–59		Jamison 1993
HepB immunization – in low-income countries with >8% prevalence	8–11		Miller, McCann 1999
Hib immunization in Asia – overall – in low-income countries	87 55	3 010 1 475	Miller, 1998
Hib immunization globally – low-income countries – middle-income countries – high-income countries	17–236 46–5 360 119–7 831		Miller, McCann 1999
TB short-course chemotherapy, Africa	3		Dejonghe
Malaria, impregnated nets, Africa	19.5		Goodman
Hypertension, different therapies, USA	4 340–87 940		Shephard
Osteoporosis, hormone replacement therapy, USA	25 244		Gabriel
Hip replacement	1 075		From Mooney, Creese in Jamison 1993
Heart transplantation	7 500		From Mooney, Creese in Jamison 1993

Table 6: Critical indicators by component

Overall system indicators:

- % of recommended vaccines being used in the immunization programme
- Proportion of districts with BCG coverage >=80%
- Proportion of districts with DTP3 coverage >=80%

Component	Planning Area	Indicators
Supply & Quality	Forecasting	Sufficient vaccines in health centres
	Procurement	Vaccines of assured quality at appropriate prices
	Production	Manufacturer viability >70%
	NRA functions	NRA functions filled appropriate to vaccine source
Logistics	Transport systems	% districts with stock-outs due to lack of availability of transport
	Cold chain	% doses lost due to failure of cold chain equipment
	Supplies distribution	% immunizations given safely and reliably
	Communication	Communication system responsive to programme needs
	Waste management	% immunization wastes disposed of in safety
Communication	Advocacy	Proportion of public dialogue on immunization issues and concerns
	Social mobilization	Proportion of civil society organizations promoting immunization of children
	Programme communication	Proportion of targeted mothers who know which disease the child was vaccinated against and when to return for next immunization
Surveillance	Routine reporting and notification	Completeness/timeliness of reporting
	Case investigation	Percent of reported cases investigated
	Diagnostic labs	Proportion of laboratories accredited or passing proficiency test
	Active surveillance	Proportion of all active surveillance sites visited according to schedule
Service Delivery	Policy development & guidelines	Availability of 3–5 year immunization plan
	Planning, co-ordination & budgeting	ICC met on routine system at least once previous year to leverage resources
	Supervision & monitoring	Proportion of districts having immunization coverage as a priority indicator
	Intervention at point of use	Proportion of districts with sufficient health workers as indicated by immunizaiton plan

From: J. Milstien et al, WHO

Table 7: Number of unreached children in low-income countries (thousand)

Birth cohort 2000	91 351
Children vaccinated in 1998	66 075
Children to reach to achieve at least 80% coverage in all countries	11 337
Children to reach to achieve more than 95% coverage	25 276

Table 8a: Estimates of immunization costs in low and middle-income countries[1]

	Birth cohort year 2000 (thousand)	**Cost at current coverage (USD million)**	**Cost to reach at least 80% coverage in all countries (USD million)**		**Cost to reach all children** (USD million)	
			Additional	Total	Additional	Total
New Vaccines:						
– 26 countries adding Hep B vaccine only[2]	68 533		157		185	
– 69 countries adding Hep B and Hib[3]	21 614		146		164	
– 43 countries adding Hep B, Hib and YF[4]	27 482		208		254	
Routine immunization with new vaccines[5]		41	511	552	603	644
Routine immunization with six traditional vaccines[6]		1 523	235	1 758	641	2,164
Total cost of increased immunization coverage	117 629		746	2 310	1,244	2,808

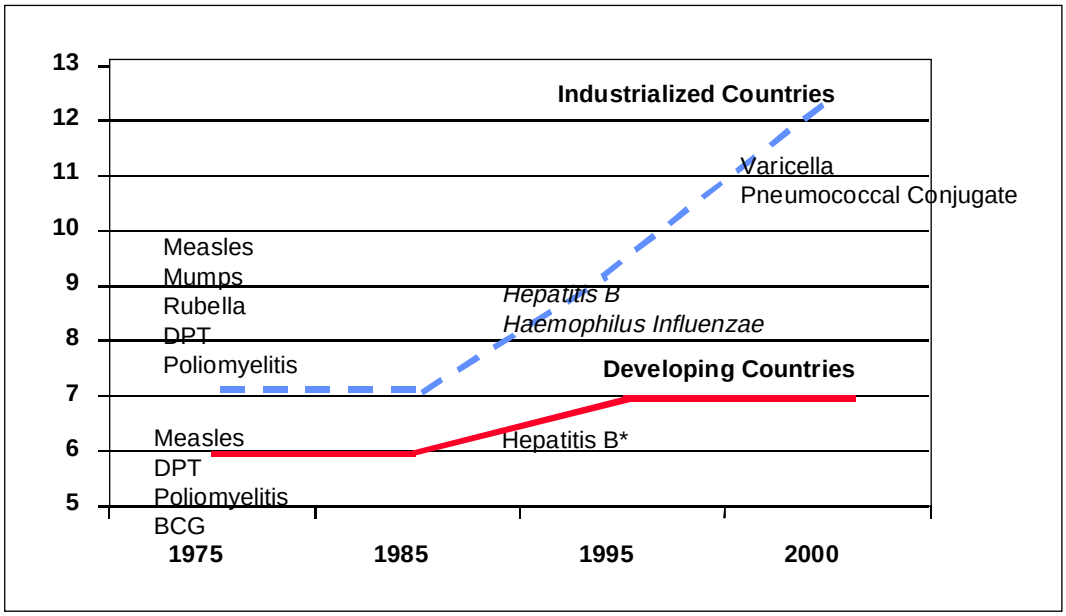
1. Equal or below GNP per capita 9 360 USD
2. Asian countries. Cost per child estimated to be 2.87 USD.
3. Cost per child estimated to be 8.50 USD.
4. African and Latin American countries at risk of yellow fever. Cost per child estimated to be 9.63 USD.
5. Introduction of Hib vaccine in all Asian countries would require an additional 333 million USD to reach at least 80% coverage and 386 million USD to reach all children.
6. Cost per child is estimated to be 17 USD at current coverage, 20 USD to reach 80% coverage and 25 USD to expand above 80% coverage.

Table 8b: Estimates of immunization costs in low-income countries[1]

	Birth cohort year 2000 (thousand)	Cost at current coverage (USD million)	Cost to reach at least 80% coverage in all countries (USD million)		Cost to reach all children (USD million)	
			Additional	Total	Additional	Total
New Vaccines:						
– 19 countries adding Hep B vaccine only[2]	64 923		151		178	
– 22 countries adding Hep B and Hib[3]	4 876		35		40	
– 33 countries adding Hep B, Hib and YF[4]	21 552		166		207	
Routine immunization with new vaccines[5]		10	352	362	425	435
Routine immunization with six traditional vaccines[6]		1 123	226	1 349	574	1 697
Total cost of increased immunization coverage	91 351		578	1 711	999	2 132

1. Equal or below GNP per capita of 1 000 USD
2. Asian countries. Cost per child estimated to be 2.87 USD.
3. Cost per child estimated to be 8.50 USD.
4. African and Latin American countries at risk of yellow fever. Cost per child estimated to be 9.63 USD.
5. Introduction of Hib vaccine in all Asian countries would require an additional 314 million USD to reach at least 80% coverage and 365 million USD to reach all children.
6. Cost per child is estimated to be 17 USD at current coverage, 20 USD to reach 80% coverage and 25 USD to expand above 80% coverage.

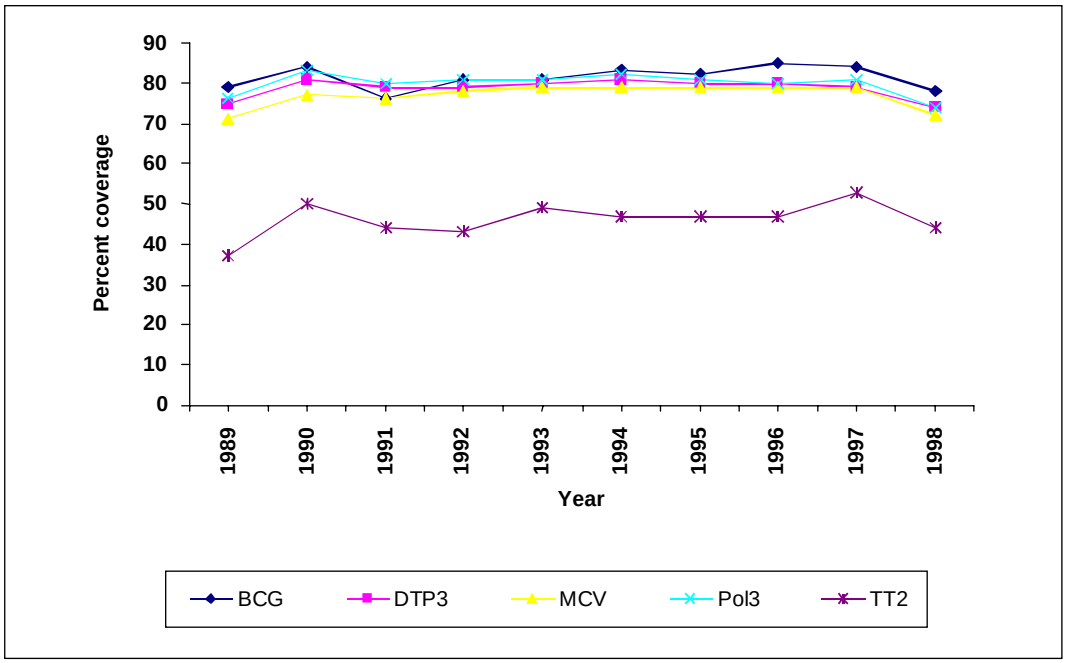
Figure 1: Number of children's vaccines routinely used in developing and industrialized countries



* Used in ~ 50% of global birth cohort

Source: World Bank

Figure 2: Global Coverage of EPI+ Vaccines, 1989 – 1998



Source: WHO Vaccine Preventable Diseases Monitoring System, 1999 Global Summary

Annex 3:
Status of the Global Fund for Children's Vaccines, January 2000

Presentation at the Second GAVI Board Meeting, 31 January 2000, Davos, Switzerland, by Mark A. Kane
Director, Bill and Melinda Gates Children's Vaccine Program.
Member, GAVI Board and Working Group

The Global Fund for Children's Vaccines (GFCV) has now been established as a functioning legal and operational entity. The Fund was put together at the request of the Global Alliance for Vaccines and Immunization to constitute one of the tools of the Alliance to promote immunization in the developing world.

The Fund was made possible by an initial contribution of $750 Million over 5 years from the Bill and Melinda Gates Children's Vaccine Program (CVP) and the Bill and Melinda Gates Foundation. The first allotment of $175 million was received in December 1999. In concert with the development of the Fund, UNICEF is developing the structures of a Working Capital Account (ultimate name and structure under consideration) at UNICEF and a procurement strategy for the Fund. WHO and the World Bank are developing assessment tools which will lead to the development of application materials for countries. A number of countries have expressed interest in being sites for early testing of these materials, and through on-going work in these countries ways to develop multi-year immunization plans and organize national inter-agency coordinating committees can be explored.

Although the Fund was announced to the press in November 1999, the major launch of GAVI and the Fund will occur at Davos 31 January 2000, in concert with major media activity in cities throughout the world. One of the major themes of the Davos Launch will be "The Children's Challenge" to mobilize the world in support of immunization. Without replacing on-going contributions for immunization the Fund is expected to be a key element and recipient of resources raised for immunization.

In addition to supporting the Fund and the Working Capital Account held by UNICEF, governments, institutions and individuals who wish to contribute financially to immunization can do so through existing mechanisms. These include direct bilateral assistance to countries and contributions to multilateral agencies involved in immunization such as UNICEF and WHO.

Many organizations may be legally constrained as to where they can send their money (for example most bilateral funds must be used at country level directly and cannot flow through the Fund, and World Bank discretionary loans must go directly to countries). However, all these resources must be co-ordinated to support the same immunization system.

Although the funding sources and routes are multiple, GAVI is dedicated to ensuring that all contributions will be used as efficiently as possible to protect the world's children against vaccine preventable diseases.

Many partners have substantially increased their immunization efforts already in response to GAVI. Additional contributions to the global immunization effort, including increased budgeting for immunization by countries themselves, increased multilateral and bilateral aid contributions, and increased development bank loans for immunization will be noted and credited by GAVI. In the future the possibility of using resources freed up by debt relief will also be explored. Support from industry in the form of direct contributions of funds or vaccines and in offering the lowest possible prices for vaccines will also be encouraged.

The US Committee for UNICEF has agreed to undertake the US fundraising efforts for the Fund and is in the process of developing a strategic fundraising plan. It will also be, in concert with UNICEF and the GAVI Secretariat, important to the participation of other National Committees for UNICEF, a number of which have expressed interest in making immunization fundraising a priority.

The US Government is considering substantial inputs, and Vice President Gore has recently announced that the administration will seek 50 million USD in next year's budget for the Fund. Senator Leahy and the Senate Appropriations Committee, as well as the Government Accounting Office and the Department of the Treasury, are very interested in this issue. Senator Leahy and the Senate Appropriations Committee will hold a hearing on GAVI and the Fund in April.

It is essential that GAVI receive funding globally. The basic structure of the Fund and resource flows were adopted at the first Board meeting as in the attached figure. The Governments of Belgium, Canada, Denmark, France, the Netherlands, Norway, Sweden, the United Kingdom, the Netherlands and the EU have been approached individually to discuss GAVI and the Fund. It is anticipated that their inputs to immunization at various levels will be increased. Potential Asian donors such as Japan or Korea have not yet been approached. A "Parliamentary Conference" in Australia is planned to be organized in order to generate interest in GAVI and the Fund in that part of the world. The need to internationalize the Fund will be high on the list of considerations in the process over the next several months when the Board of the Fund will be organized and an Executive Director recruited.

Administrative update

1) On 2 December 1999, the Application for Recognition of Exemption under Section 501 (c) 3 of the Internal Revenue Code (Form 1023) was submitted. The IRS responded positively on 30 December 1999. At this time, the interim Board of Directors was comprised of Mark Kane and Gordon Perkin. It has been suggested that the President of the US National Committee for UNICEF and the Executive Secretary of GAVI join the interim board.

2) The Fund has retained Merrill Lynch to act as its interim investment broker.

3) An interim investment policy for the Fund was adopted on 28 December 1999, which outlines a conservative investment approach emphasizing preservation and safety of capital and diversification of risk. Investments should be ethical and consistent with the Fund's purpose to improve the health of children in

developing countries. The Fund's investment portfolio will be reviewed regularly by an independent investment professional.

4) A disbursement of 175 million USD from the Gates Foundation to the Global Fund was received at Merrill Lynch on 16 December 1999 and invested into their Premier Money Market Fund. Following a meeting of the interim Fund Board on 21 December, the funds were diversified on 22–23 December into high-grade commerical paper and government bonds.

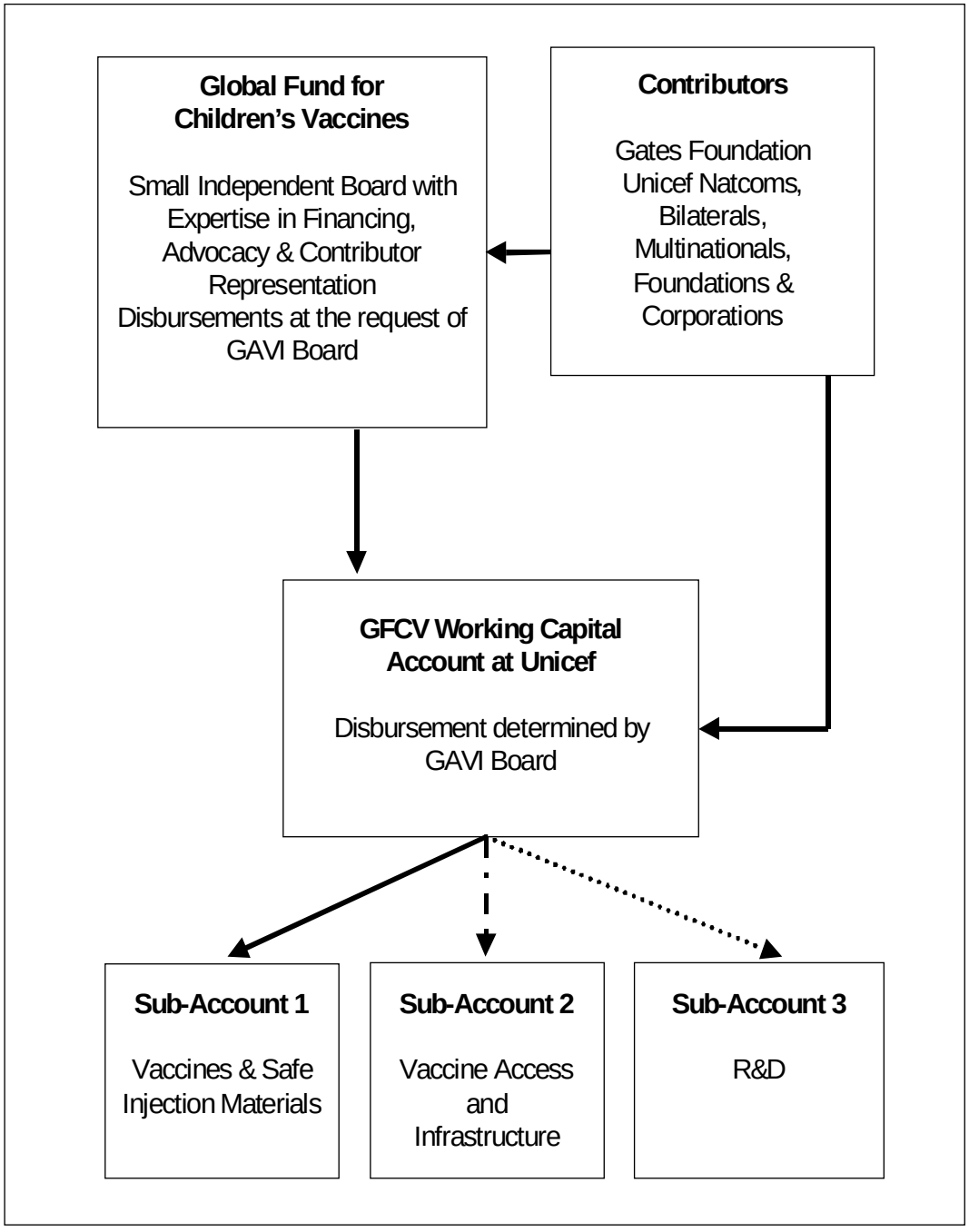
5) A relatively small amount (less than 2 million USD) was kept in money market account to support the ongoing operational costs of the Fund. This includes lawyers' and accountant fees as well as support to the US Committee for UNICEF for the development of a strategic fundraising plan.

6) An independent accounting firm, Clark Nuber, has been retained to provide a range of services including monthly bookkeeping, tax preparation, annual audit, and consulting on IRS compliance issues.

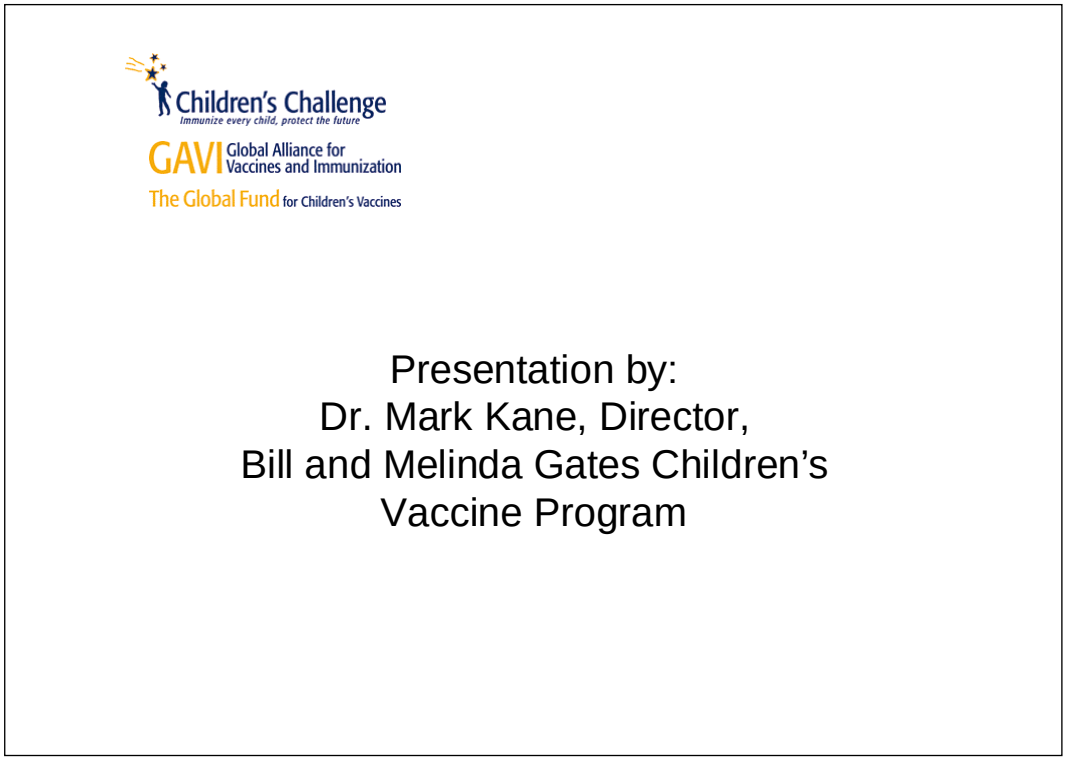
7) During the start-up period, CVP and PATH staff will provide administrative and financial support to the Fund, supported by CVP funds. This will include an interim administrator and programme assistant (provided by CVP), assistance with investment oversight, as well as general technical assistance for establishment of a non-profit organization.

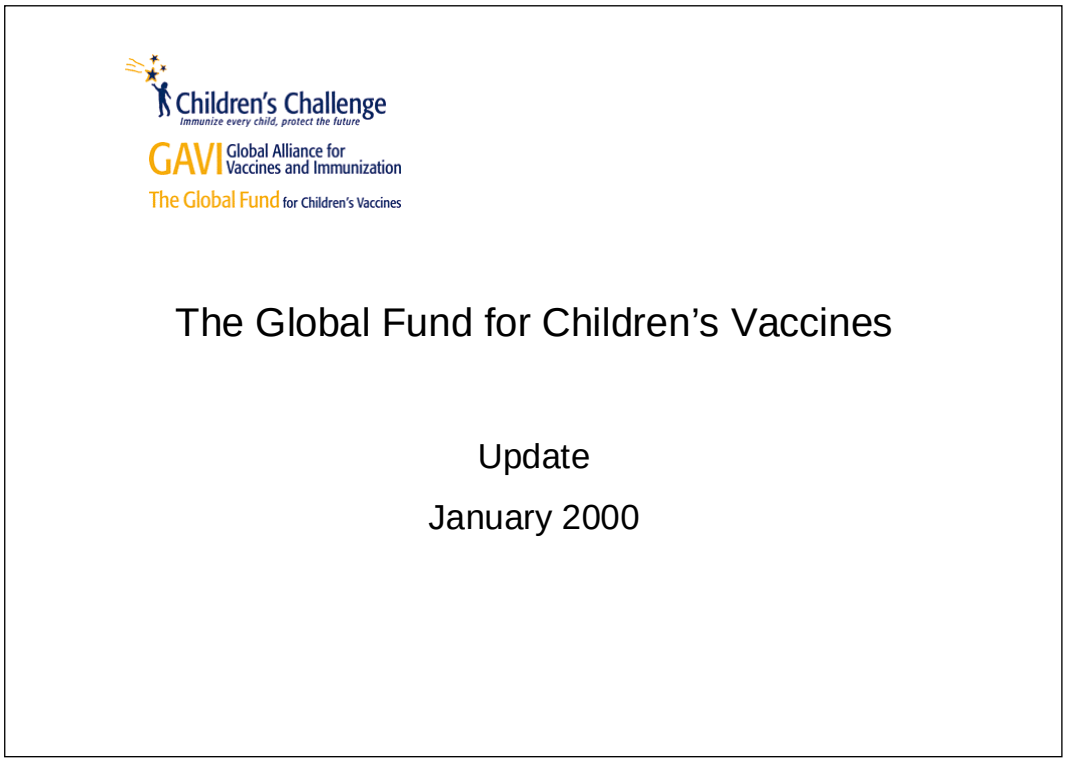
8) A decision on location and recruitment of fulltime staff (Executive Director, Administrator, Program Assistant) for the Fund, as well as on the full expansion of the Board of Directors, is expected to occur during the next few months, in concert with the development of the strategic fundraising plan. Once the Board of the Fund is established in consultation with the GAVI Board, all decisions taken to date may be modified or changed by the Board of the Fund. All of this should be in place by the June GAVI Board meeting so that procurement of the first vaccines can be made by the middle of 2000.

Figure 1: Structure - Global Fund for Children's Vaccines



Reproduction of a slide presentation





Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

The Fund Exists as a legal entity and currently contains $175 million from the Bill and Melinda Gates Foundation

All decisions taken to date on behalf of the fund are interim and can be completely modified or reversed by the Board of the Fund once officially constituted

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

Country level work has already begun in a number of countries to test the tools to be used for the assessment and application process and to gain experience with national immunization coordinating committees, multi-year immunization plans, and use of other financing mechanisms to support the plans

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

Window 1 (new and underused vaccines),as approved by the Board, will be in operation by mid 2000

Window 2 (access and infrastructure)is in the process of being developed by the WG and a wide consultative process

Window 3 is under discussion

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

Fundraising will occur at many levels

Global fundraising will occur for the GFCV and funds will be directed to the US account 50(c)3 or to the Working Capital Account at UNICEF (name under discussion) depending on the needs of the donor

Funds can also flow to partners and at country level (bilateral)

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

Increased country budget lines for immunization, bilateral aid to countries for immunization, Development Bank loans for immunization and in kind contributions (eg industry donations of vaccine) will be considered responses to Children's Challenge

The US Fund for UNICEF is developing a fundraising plan for the US

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

Discussions on GAVI and The Fund have already been held with major donor governments and National Committees for UNICEF

(Australia, Belgium, Canada, Denmark, EU, France, Norway, The Netherlands, Sweden, UK, USA)

Letter from Dr Brundtland to Governments

Update
January 2000

We are now in the process of collecting names for candidates for Membership on the Board of the Fund and for Executive Director

These individuals will be vetted and approved by the GAVI Board

Representatives of Major Donors

Financial Experts

Public Figures

Public Health Experts

GAVI Executive Secretary

Update
January 2000

The function of the Fund Board will be to advise on and approve investment policy, actively participate in Fundraising, and ensure that funds are used to support immunization of children in developing countries

The Fund Board will not oversee technical issues, which is the function of the GAVI Board

The Fund Board will approve release of funds on request of the GAVI Board

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

On December 2, 1999, the Application for Recognition of Exemption under Section 501 (c) 3 of the Internal Revenue Code (Form 1023) was submitted. The IRS responded positively on December 30, 1999. At this time, the interim Board of Directors was comprised of Mark Kane and Gordon Perkin. It has been suggested that the President of the US National Committee for UNICEF and the Executive Secretary of GAVI join the interim board.

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

The Fund has retained Merrill Lynch to act as its interim investment broker.

An independent accounting firm, Clark Nuber, has been retained to provide a range of services including monthly bookkeeping, tax preparation, annual audit, and consulting on IRS compliance issues.

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

An interim investment policy for the Fund was adopted on December 28, 1999, which outlines a conservative investment approach emphasizing preservation and safety of capital and diversification of risk. Investments should be ethical and consistent with the Fund's purpose to improve the health of children in developing countries. The Fund's investment portfolio will be reviewed regularly by an independent investment professional.

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

A disbursement of $175 million from the Gates Foundation to the Global Fund was received at Merrill Lynch on December 16, 1999 and invested into their Premier Money Market Fund. Following a meeting of the interim Fund Board on December 21, the funds were diversified on December 22 and 23 into high-grade commercial paper and government bonds.

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

A relatively small amount (less than $2 million) was kept in money market account to support the ongoing operational costs of the Fund. This includes lawyers' and accountant fees as well as support to the US Committee for UNICEF for the development of a strategic fundraising plan.

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

During the start-up period, CVP and PATH staff will provide administrative and financial support to the Fund, supported by CVP funds. This will include an interim administrator and program assistant (provided by CVP), assistance with investment oversight, as well as general technical assistance for establishment of a non-profit organization.

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

A decision on location and recruitment of fulltime staff (Executive Director, Administrator, Program Assistant) for the Fund, as well as on the full expansion of the Board of Directors, is expected to occur during the next few months, in concert with the development of the strategic fundraising plan.

Children's Challenge
Immunize every child, protect the future
GAVI Global Alliance for Vaccines and Immunization
The Global Fund for Children's Vaccines

Update
January 2000

Once the Board of the Fund is established and approved by the GAVI Board, all decisions taken to date may be modified or changed by the Board of the Fund. All of this should be in place by the June GAVI Board meeting so that procurement of the first vaccines can be made by the middle of 2000.

Annex 4:

Update of activities of a pre-task force on research and development of GAVI, including a meeting jointly organized with the WHO Intercluster Vaccine Research Initiative, 4–5 November 1999, Geneva, Switzerland

Presentation at the Second GAVI Board Meeting, 31 January 2000, Davos, Switzerland by Amie Batson and Michael Levine

Summary and items for action

Recognizing that "Accelerating the research and development efforts for vaccines and related products specifically needed by developing countries, particularly vaccines against HIV/AIDS, malaria and tuberculosis" is one of the fundamental objectives of the Global Alliance for Vaccines and Immunization, the purpose of this pre-Task force on Research and Development meeting was to:

1) Define the type of vaccines, in addition to those for AIDS, malaria and tuberculosis, that should be targeted by GAVI and prioritized for development;

2) Identify the gaps that exist globally which are preventing these vaccines from being developed or are delaying their development;

3) Prepare a preliminary broad strategy to begin to address the gaps with solutions.

Observations and recommendations

The following observations and recommendations were made:

- GAVI should foster research and development of developing market vaccines against diseases for which the burden is largely limited to the developing countries.
- A task force on research and development should be established to join the other three task forces that assist the GAVI Secretariat and working group to achieve GAVI's objectives.
- The GAVI Task Force on Research and Development should work with WHO, epidemiologists from developing countries, industry, UNICEF, World Bank and other partners to set the priorities for which developing market vaccines, in addition to those for HIV, malaria and tuberculosis, are most needed.
- Where epidemiologic, microbiologic or parasitologic data are deemed to be insufficient to allow a fair assessment of disease burden, the collection of those data should be undertaken.
- The GAVI Task Force on Research and Development should "push" the development of these vaccines by:

  - fostering partnerships with industry;
  - assisting in obtaining patent protection;
  - providing access to pilot lot formulations (through various mechanisms);
  - facilitating sponsorship (i.e., financial support) for clinical trials;
  - exploring ways to make clinical trials simpler and more economical;

- The global capacity for production of pilot lot formulations of different types of vaccine under GLP and GMP should be catalogued (and periodically updated).
- The Task Force on Research and Development should, in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID), should review future issues of the Jordan Report to ensure that research progress on the GAVI priority vaccines is contained therein.
- The GAVI Task Force on Research and Development should oversee the preparation of a catalogue of clinical trials facilities in industrialized and developing countries with experience or potential for evaluating developing market vaccines in Phase 1–IV clinical trials. (This must be annually updated).
- GAVI should strengthen the clinical trials research units in Africa, Asia, and Latin America that have established track records in performing GCP clinical trials in adult and pediatric populations and should facilitate the establishment of necessary new sites (e.g., for testing tuberculosis vaccines).
- Non-profit companies and "virtual corporation models are attractive strategies to be pursued for nurturing the development of specific developing market vaccines.
- More direct forms of academia/industry partnership should also be encouraged.
- The GAVI Task Force on Research and Development should actively explore opportunities in large developing countries such as China, India, Brazil and Indonesia that have large-scale manufacturing capacity and strong research capability.
- The "push" activities of the GAVI Task Force on Research and Development should be coordinated with the "pull" efforts of the GAVI Task Force on Financing to achieve synergy.

Co-Chairs:

Professor M. M. Levine, GAVI Working Group and University of Maryland

Dr Jeffrey Almond, Aventis-Pasteur

Dr Frances André, SmithKline Beecham

Rapporteur:

Dr Carole Heilman, National Institute of Allergy and Infectious Diseases

WHO Intercluster Vaccine representative:

Dr Teresa Aguado

Background

The Global Alliance for Vaccines and Immunization (GAVI), a newly formed coalition in which the principal partners include representatives of the developing countries of the world, the World Health Organization, UNICEF, the World Bank, industry, bilateral agencies, the Gates Childrens Vaccine Program and the Rockefeller Foundation, was launched within the United Nations system in October 1999. The five major objectives of this Alliance are:

- Improving access to sustainable immunization services;
- Expanding the use of all existing safe and cost-effective vaccines;
- Accelerating the development and introduction of vaccines;
- Accelerating the research and development efforts for vaccines and related products specifically needed by developing countries, particularly vaccines against HIV/AIDS, malaria and tuberculosis;
- Making immunization coverage a centrepiece in the design and assessment of international development efforts, including deep debt relief.

To begin to address the objective of accelerating the development of vaccines of particular importance for developing countries, a Pre-Task Force Meeting was convened in Geneva on November 4 and 5 1999, co-sponsored by GAVI and by the Intercluster Vaccine Research Initiative of the World Health Organization. The purpose of this pre-task force meeting was to:

1) Define the type of vaccines, in addition to those for AIDS, malaria and tuberculosis, that should be targeted by GAVI and prioritized for development;
2) Identify the gaps that exist globally which are preventing these vaccines from being developed or are delaying their development;
3) Prepare a preliminary broad strategy to begin to address the gaps with solutions.

Vaccine development in the last two decades of the 20th century

In the last two decades of the 20th century extraordinary advances in biotechnology were applied in the area of vaccine development, resulting in the licensure of exciting new vaccines such as *Haemophilus influenzae* type b (Hib) conjugates, acellular pertussis, recombinant hepatitis B and attenuated varicella. Although most of the basic scientific breakthroughs that made these vaccines possible were generated in public sector (academic and government) research institutions, most of the cost for their clinical development, including the support of extensive phase II and III clinical trials, was borne by the big pharma vaccine industry in industrialized countries. An investment of several hundred millions dollars was typically required to bring each of these new vaccines to licensure. For this reason, within the first few years after licensure and commercialization of those products, their unit price remained high, as companies sought to recoup their large investments through sales in wealthy, industrialized country markets. In recent years, the need to assure a return on investment and avoidance of risk has influenced the decisions industry has made with respect to investing in research and development for future products.

Vaccines for which research and development activities are falling behind

Vaccines for which research and development are falling behind can be conveniently divided into two main categories, impeded vaccines and developing market vaccines.

Impeded Vaccines

These are candidate vaccines that would almost certainly have substantial markets in industrialized countries but certain scientific, ethical or public perception obstacles dissuade the vaccine industry from making investment in their development a high priority. For example, the fear that M protein-based vaccines against Group A *Streptococcus pyogenes* and vaccines against respiratory syncytial virus (RSV) might elicit serious adverse reactions has stifled the pace of their development, despite the likelihood of large markets for these vaccines in industrialized countries.

Developing market vaccines

Developing market vaccines lack substantial markets in industrialized countries but offer potential markets in developing countries.

There are a number of diseases for which the burden is prominent in developing country populations but little if any risk is posed for individuals in industrialized countries unless they travel to developing areas. Certain bacterial diseases (e.g., *Shigella* and enterotoxigenic *Escherichia coli* infections, cholera, typhoid fever and group A meningococcal infections), viral diseases (e.g., dengue fever, hepatitis E) and parasitic infections (e.g., malaria, leishmaniasis and schistosomiasis) provide examples. The fact that industrialized country markets are either lacking or are limited to travellers has heretofore provided little incentive for industry to make the large investments necessary to finance the clinical development of these vaccines. Henceforth, for reasons of brevity, such vaccines will be referred to as "developing market" vaccines. This term will reflect that these vaccines are particularly targeted for use in developing countries and will also convey the notion that non-traditional markets will have to be developed for these vaccines in those countries. For example, whereas in industrialized country markets industry may rely on a low volume/high margin approach, profitability of "developing market" vaccines in less-developed countries will likely require adoption of a high volume/low margin approach.

Defining the vaccines of interest to the research and development component of GAVI

It was agreed that, at least initially, a GAVI Task Force on Research and Development should focus its efforts on fostering the development of developing market vaccines critically needed by developing countries.

Prioritizing specific vaccine projects in which GAVI should be involved

GAVI's involvement in championing the development of vaccines against AIDS, malaria and tuberculosis is specifically instructed in its charter. Deciding what developing market vaccines should draw the additional focus of GAVI will depend on consideration of a number of factors, including:

- The magnitude of the disease burden;
- The public perception of the disease and of the need for its control;
- Whether the science is sufficiently mature to generate rational vaccine candidates;
- Whether vaccine candidates are already in clinical trials or are approaching being ready for transition to clinical trials;
- Microbiological/parasitical factors (e.g., whether multiple serotypes or antigens from different stages of the parasite must be included in the vaccine);
- Whether alternative public health control measures are available;
- Whether an effective treatment exists;
- Whether the disease has the potential to cause epidemics and pandemics;
- Whether there exists a travellers' market for the vaccine in industrialized countries;
- Whether the vaccine can be combined or concomitantly delivered with other vaccines through existing immunization services;
- Whether the vaccine has characteristics that are particularly attractive for use in developing countries such as non-parenteral (e.g., mucosal or transcutaneous) administration, an immunization schedule that requires only 1–2 doses, and effectiveness in infants;
- Estimates of the cost-effectiveness of the vaccine, assuming optimal implementation.

To obtain preliminary information in an informal manner, the participants were asked to respond to a questionnaire asking them to rank vaccine development priorities for bacterial, viral and parasitic developing market vaccines, taking into consideration the above criteria. The results of this informal survey are summarized in Table 1. It was agreed that during the next year, in collaboration with the WHO Intercluster Vaccine Research Initiative, a GAVI Task Force on Research and Development must undertake a detailed, systematic analysis to select a few initial priority vaccines to be fostered, in addition to AIDS, malaria and tuberculosis, taking into consideration all of the above-mentioned criteria.

GAVI push strategies for fostering research and development of developing market vaccines

The GAVI Task Force on Financing is addressing "pull" mechanisms to encourage industry to invest in the development of developing market vaccines that would primarily be used in the developing world. Accordingly, the Pre-Task Force on Research and Development concluded that it should address push mechanisms by which the public sector, working in conjunction with the private sector, can facilitate the development of developing market vaccines. Ideally, these pull and push mechanisms would complement one another to synergize the development of developing market vaccines.

There is precedent for the success of push mechanisms. The public sector largely financed the development of four developing market vaccines that became licenced by regulatory agencies in many countries. These vaccines, for which the industrialized country market is essentially limited to travellers, include:

- Ty21a live oral typhoid vaccine
- Vi capsular polysaccharide parenteral typhoid vaccine;
- B subunit/inactivated whole cell combination cholera vaccine, and;
- CVD 103-HgR live oral cholera vaccine.

Identifying specific gaps in the global capability for research and development of developing market vaccines

The GAVI Pre-Task Force focused on identifying the gaps and barriers faced by relevant current vaccine development programmes. It is anticipated that this information can allow strategies to be devised to remove the hurdles, thereby accelerating the vaccine development programmes.

Are currently available disease burden data adequate to direct vaccine development activities?

Disease burden may be quantified with respect to morbidity, mortality, or certain epidemiologic currencies such as disability-adjusted life years (DALYs), quality-adjusted life years (QALYs) or years of potential life lost (YPLLs). It was generally acknowledged that large gaps exist in the quality of disease burden data.

Burden of Shigella disease as a model. A recent publication (K Kotloff et al, Global burden of Shigella infections: implications for vaccine development and implementation of control strategies. Bull WHO 77:651–666, 1999), that describes in detail an exercise to estimate the global burden of diarrheal disease and dysentery caused by Shigella, was used to illustrate the complexities, limitations and advantages of such an exercise. This was deemed to be a particularly useful example because the main clinical syndromes caused by Shigella, diarrheal disease and dysentery, are also caused by a number of other enteric pathogens. Moreover, it is an antigenically diverse pathogen, as there are four species and 37 serotypes and sub-types of Shigella. Therefore, adequate microbiologic as well as epidemiologic data are needed to estimate the global disease burden of Shigella. The burden of Shigella infections was calculated separately for developing versus industrialized countries. In this comprehensive exercise, the global burden was calculated with respect to deaths, severe cases (requiring hospitalization), moderate cases (seen as outpatients in treatment centres) and mild cases (that do not seek health care). Since both the incidence of Shigella disease and mortality disproportionately affect certain age groups, the burden was calculated separately for relevant age strata: < 1 year, 1–4 years, 5–14 years, 15–59 years, and ≥ 60 years of age. Serogroup and serotype data needed to direct vaccine development strategies were analyzed in relation to different geographic areas. Finally, a sensitivity analysis was performed to estimate the high and low range of cases and deaths. A summary of the global burden of Shigella,with the low and high estimates, is shown in Table 2.

The exercise to estimate the global burden of Shigella revealed several factors relevant to assessing the burden of several other diseases of interest to GAVI. The first was the surprising paucity of available data on the incidence of diarrheal disease among adults in developing countries. Whereas prospective paediatric cohort studies in multiple sites in the developing world have documented the number of episodes of diarrheal disease per child per year in infants, toddlers and pre-school children, analogous data for adults simply do not exist. Another, revelation was the dearth of epidemiologic and bacteriologic data from Africa, in contrast with Asia and Latin America. Finally, it was noted that many of the centres of excellence in Asia and Latin America where clinical trials of various vaccines have been carried out during the past two decades are also sites where the most comprehensive epidemiologic and microbiologic data on diarrheal disease were generated. These sites include the International Center for Diarroeal Disease Research, Bangladesh (ICDDR,B) and the Centro para Vacunas en Desarrollo, Chile (CVD-Chile).

Institute of Medicine model. A model in which QALYs were used as a common epidemiologic currency was presented as an implement to guide the setting of vaccine development priorities. This model was recently utilized by the IOM (Institute of Medicine) as a proposed tool for decision-making. When utilized to assess the vaccine needs for the United States, and considering possible therapeutic as well as preventive uses of vaccines, four levels of vaccine priorities were established which reflected differences in cost/QALY saved. The details of this model, as well as the vaccines identified in each of these categories can be found at http://www2.nas.edu/hpdp/.

Disease burden in perspective. Despite the paucity of precise burden data for many diseases, it was agreed that the precision required will depend on how the data are to be used. Arguably, even the currently available imprecise disease burden estimates can allow a preliminary setting of priority among competing vaccine projects, since other equally important factors besides disease burden must be considered. However, the general need to improve both epidemiologic and microbiologic surveillance in sub-Saharan Africa was noted. Representatives of the private sector remarked that for them estimates of the global and regional burdens of disease were important to establish priorities internally, and would influence whether they would collaborate with GAVI in pushing the development of certain developing market vaccines. It was generally agreed that, at least for tuberculosis, malaria and HIV/AIDS, current disease burden data were sufficient to validate their high priority as a focus of GAVI. Diarrheal diseases, acute lower respiratory infections and parasitic infections have been recognized as important public health targets for intervention. For diarrheal diseases adequate data exist from studies in developing countries to incriminate the most important pathogens. Data to attribute bacterial and vial etiologies to lower respiratory infections are more tenuous because of the difficulty in obtaining relevant clinical specimens for microbiologic analysis. Indeed, experience with Hib conjugate vaccine in The Gambia and Chile suggests that vaccine probe studies that measure the difference in hospitalization rates for pneumonia in vaccinated infants versus controls provide the most accurate (as well as relevant) measure of specific disease burden. For parasitic diseases other than malaria the quality of the data varies by geographic region and by infection. Thus, there is a need for well-designed systematic surveys to generate more precise burden data.

Is there adequate monitoring of the status of vaccine development activities globally?

Information for the general public. General information about the status of existing and the prospects for new vaccine research programmes globally is made available in a form suitable for the educated lay public in the WHO publication "State of the World's Vaccines and Immunization". An updated version is being prepared for publication in the year 2000. This monograph provides a useful "broad brush" review that promotes public support for vaccine programmes.

Specific technical information. Detailed information on vaccine research is provided in the annual Jordan Report prepared by the staff at the National Institute of Allergy and Infectious Diseases, NIH, USA. This was considered by all participants to be a "model publication". However, there was some concern that the Jordan Report might be incomplete, particularly with respect to research activities in developing countries. It was agreed that several experts identified by GAVI will review the Jordan Report for potential gaps. A Jordan Report supplemented in this manner could serve the broader global audience that GAVI must target.

Broad strategies for implementing push mechanisms to facilitate and expedite prioritized vaccine development projects

The group concluded that two likely scenarios might result in accelerated development of priority developing market vaccines. Both involve public/private partnerships. They include:

- Public sector partnering with "big pharma" in industrialized countries
- Public sector partnering with industry in large non-industrialized countries that have a sophisticated vaccine industry (e.g., India, Brazil, Indonesia, China).

Whereas both approaches could be useful and should be pursued, many considered that the former would be ideal if it could be achieved. Much discussion thereupon focused on what would be required to entice major vaccine manufacturers to become intimately involved in accelerated joint development projects for developing market vaccines. From the animated and highly productive discussions that ensued on this theme, in which both public sector and industry representatives actively contributed, the following points were noted:

- Each vaccine selected should have intellectual property coverage which the partnering company would licence;
- If the vaccine has a potential market among travellers in industrialized countries it would be more attractive to industry;
- The public sector would have to convincingly quantify the extent to which the vaccine would be used in developing countries so that the requirements for production facilities can be matched with the projected markets in those countries;
- The costs of preparing early pilot lot formulations may have to be either entirely borne by the public sector or shared on a disproportionate basis with the public sector paying the majority;

- Expenses for carrying out the early Phase I and II clinical trials, when the risk of failure is highest, (i.e., when odds are highest that the vaccine may prove to be unacceptably reactogenic or inadequately immunogenic), would have to be borne by the public sector;
- The public sector would have to contribute substantially to the costs and to performance of the pivotal pre-licensure Phase III efficacy trial, including site preparation.

If the public sector assumes the high-risk portions of the development costs of a vaccine, once it is licenced by regulatory authorities and manufactured on a large scale, the unit price of the vaccine in developing countries (as opposed to the price for travellers) should reflect the limited investment in R&D for that vaccine by the company (much of the costs will have been borne by the public sector partners).

Non-profit companies and virtual corporations. One attractive approach to create symbiotic public–private partnerships to develop developing market vaccines is to establish a not-for-profit (NFP) company, funded by the public sector.

The NFP company would be dedicated to foster development of the specific vaccine to the point of licensure and assure manufacture of sufficient vaccine for use in developing countries. Since such a company would focus on development of a single product, there would be no competing internal projects of higher priority. The NFP company would also have the freedom to design the product specifically for use in a developing-country setting, rather than adapt a product originally designed for an industrialized country.

Such a partnership can take several forms. The fastest and most efficient approach would be to form an alliance between the NFP company and an industrial vaccine manufacturer. Vaccine development could proceed on a fast track. Once pilot formulations are available, studies could rapidly move into target populations in developing countries. When more definitive formulations become available after scale-up, the fill, release, quality control and clinical, regulatory and licensure activities for the vaccine could be the responsibility of the NFP company; these activities would not compete for internal resources of the commercial company.

The International AIDS Vaccine Initiative (IAVI) serves as a model of a virtual corporation. While IAVI is a not-for-profit entity committed to AIDS vaccine development, it is managed in a private sector style and operates in a business-like manner. For each specific task in the AIDS vaccine development process, IAVI seeks a suitable academic group or company with a track record of expertise in that area and contracts their services.

Are there substantial gaps in the global capacity to obtain pilot formulations?

Participants agreed that there exist two broad classes of pilot lot formulations. One is adequate for undertaking proof of principle Phase I and early Phase II studies to establish the safety and immunogenicity of the vaccine candidate. Such formulations may not be readily amenable to subsequent scale-up. The other encompasses more sophisticated formulations prepared with considerable aforethought to possible subsequent scale-up to prepare large lots for a Phase III trial and eventual consistent large-scale manufacture.

Regulatory issues relevant to pilot lots. The regulatory requirements and guiding principles for pilot lot production from the perspective of the US Food and Drug Administration (FDA) were presented as a general approach of regulatory agencies. The regulations require that biological products manufactured for human use, including material for clinical trials, be manufactured in accordance with the current recommendations for Good Manufacturing Practices (GMPs). However, regulatory agencies recognize that it may not be possible to meet full GMPs when manufacturing preparations for early small (e.g., Phase I) clinical trials. Nevertheless, there should be sufficient controls, oversight and testing in place to assure reproducibility of the process and the safety of the product prepared at a licenced facility. The comparability of early pilot lot material to subsequent scaled-up formulations produced under stringent GMPs would have to be verified.

How do public-sector vaccine-research groups and small vaccine biotechnology companies obtain pilot lot formulations?

Within the U.S.A., a network of pilot lot facilities that specializes in various platform technologies is supported under contract by the NIAID, NIH. Priority is given to HIV and malaria vaccine development.

The U.S. Department of Defense (DOD) also supports production of candidate vaccines primarily through the Walter Reed Army Institute of Research (WRAIR) facility.

Several public sector in-country producers of national vaccines were described. The Nordic Public Health laboratories/institutions were originally established to provide vaccines for national use. Recently, however, increased production costs have made small-scale production unprofitable. The institutes have responded to these changes in different ways including privatization (Sweden); expanding to include export capability (Denmark) or preparing to close (KTL -Finland). Each of these facilities may be available for pilot lot production assuming, in the case of KTL, that the facility can be maintained. RIVM, in the Netherlands, produces pediatric vaccines primarily for local use. This facility is a member of the WHO Global Training Network and has a tradition of sharing vaccine development expertise with developing countries. Such expertise is currently being developed in Indonesia and Vietnam. A new member of this Network, the International Vaccine Institute (IVI) based in Seoul Korea, is planning to construct a pilot lot production facility (expected to open in 2002) that will have the capability for making both bacterial and viral vaccines. Planned associated research facilities will include an animal facility and clinical testing capability.

Peptide Therapeutics/Oravax, representing small vaccine biotechnology companies, described their pilot lot capability as virtual. Products of interest are developed/ licenced and through partnerships, clinical lots of vaccines are produced.

How large industrial vaccine manufacturers provide pilot lot formulations for lower priority projects

Descriptions of the capacity and prioritization for pilot lot production by large vaccine companies echoed a common theme. Namely, there is fierce competition internally within companies to have pilot lots produced of contending candidate vaccine projects. Moreover, depending on the specific vaccine, the costs for production of the pilot formulation may be quite high. In addition to process development, issues such as consistency, stability and strict quality control are incorporated into every pilot lot. Within companies, vaccines with the highest probability of success are given high priority for development, including facilitated access to pilot lots.

How do vaccine research groups in developing countries gain access to pilot lots of their vaccine candidates?

Several illustrative examples were given of pilot lot capacity in developing countries. The Hong Kong Institute of Biotechnology, a private, non-profit manufacturing and technology centre that has been in operation since 1997, has, under contract, prepared pilot lot formulations of both malaria and schistosomiasis vaccines under GMP conditions. Facilities in Viet Nam and similar institutes of biological products in several cities in China manufacture EPI vaccines, as well as Hepatitis B, Japanese B encephalitis, and Vi polysaccharide parenteral typhoid vaccines. The National Institute of Hygiene and Epidemiology in Hanoi, Viet Nam, locally produced an inactivated oral cholera vaccine that was evaluated in a large-scale field trial. Special efforts are ongoing to meet GMP standards at that Vietnamese facility as well as to strengthen the capability of national control authorities.

Salient summary points on pilot lot formulations

This survey of representative groups revealed that:

- The difficulty in obtaining pilot lot formulations of candidate vaccines is one of the most serious and prevalent obstacles facing public sector (and to a lesser degree private sector) researchers who want to transition their research on developing market vaccines into the clinical arena where Phase I clinical trials can be initiated.
- Pilot lot production facilities to make relatively simple formulations under GLP or GMP, of the class adequate for Phase I proof of principle trials, exist worldwide.
- Access to pilot lot facilities comes with certain constraints and at high cost.
- The pilot lot production is costly due in large part to the regulatory standards for use of biologic products in humans.
- Although many facilities are available, worldwide, all have competing priorities.
- Whereas there are a few full-service facilities, most units are limited to a few platform technologies. For unique or complex vaccines, there is often a paucity of people trained in this specialized science.
- There is a pressing global need for more bio-engineers skilled in both the ability to prepare high quality pilot lot formulations and who can then guide scale-up.

- One of the best models for priority product development is to partner with industry at a point when sufficient information is available to argue credibly for the probable success of the vaccine candidate.

Successful precedent. The four developing market vaccines (two typhoid and two cholera) that became licenced products in the last 15 years were the result of public–private partnerships. The public sector incurred most of the costs for the Phase I-III clinical trials, whereas the industrial partners provided formulations of the vaccine for the critical clinical trials. Without these partnerships, these vaccines would not have become licenced products and public health tools, or the pace of their development would have been much slower.

Alternative innovative strategies for accessing pilot lot capacity: To devise ways to increase the access to pilot lot formulations for research teams working on developing market vaccines of interest to GAVI, three models were discussed.

A GAVI/Industry collaborative facility. This could be either a "virtual" or a real institute, or both, depending on the specific vaccine development projects. Such a GAVI/industry facility would be limited to producing pilot lots of developing market vaccines of little interest to industry. However, because of the complexity of product development, this facility should be managed by individuals with industry experience. One possibility would be that every major vaccine company would sponsor a development project, putting a senior development person at the disposal of the institute as an expert to follow up a particular project. One could envision professionals hired by the institute or put by the companies at the disposal of the institute as a kind of "sabbatical". Operational costs would have to be contributed by GAVI's partners.

Close collaboration with scientists of the original discovery group would be required for success.

A non-profit, self-supporting GAVI facility. A second scenario involves the acquisition of a facility using private funds and managed by a private contractor. The facility would be self-supporting but non-profit. A scientific advisory board would guide the vaccine development decisions and an advisory committee composed of industrial scientists would provide practical guidance, and perhaps future interest in products developed under this concept.

Public/private collaborations. The third model is based on private/public partnerships between academia and industry. Academia would receive funding for the development of vaccine candidates in partnership with industry. Intellectual property rights developed during the partnership would revert to the funding body if milestones were not met. A royalty arrangement would also be developed that would benefit the funding agency.

There was agreement that solving the problem of access to pilot lot formulations is one of the most important generic obstacles that GAVI should address in its research and development agenda. There was also a consensus recommending that a GAVI Task Force on Research and Development should explore the various options in greater depth.

Identifying generic gaps in the research and development capability: clinical trials

Good Clinical Practice guidelines. The harmonization and codification of good clinical practice guidelines is a major advance that provides a framework for clinical trials to be comparably performed globally. However, in practice, the question of balance was raised with respect to the amount of clinical data to be collected during clinical trials and its documentation. Globally, one sees two broad approaches to performing clinical trials, with respect to the amount of data collected and the monitoring of the data. In general, nowadays, when industry undertakes Phase II clinical trials an inordinate amount of clinical data is often collected. An evaluation of the types of information requested for critical path (for licensure) Phase II clinical studies sponsored by industry suggested that up to 80% of the time spent by clinical trial nurses is devoted to investigating and recording adverse events (e.g., common cold) that are not relevant to the vaccine, and concomitant medications. Clinical and laboratory data collected during a Phase II trial must be monitored and statistically analysed. Industry typically hires contract research organizations (CROs) to monitor and audit the data. Indeed, within the past decade CROs have themselves become an industry. This approach inflates the cost of industry-sponsored Phase II studies. Up to 30% of the costs of the clinical development stage of a vaccine may be spent on monitoring the clinical data. Obviously, industry will aim to recoup these costs.

By necessity, a different approach is followed by experienced public sector investigators who, while also adhering to GCP guidelines, perform similar Phase II clinical trials at a fraction of the expense. This is accomplished by carefully limiting the collection of data to what is relevant, using simplified case report forms, and by utilizing internal monitoring and auditing. To many investigators who perform clinical trials, it appears that the time has come to undertake a fundamental review to consider how to make clinical trials more rational and economical with regard to information. The concern is not only balance but also the effect of imbalance (e.g., compromising the recording of relevant data). Inordinate time spent on documenting events of questionable relevance and the collection of data of questionable clinical value greatly add to the costs of performing clinical trials.

In future in the case of public/private collaborations in which the public sector will be carrying out the clinical trials, there will have to be agreement beforehand on how the trials are to be conducted. Economy can be achieved if the protocol is designed with attention to avoid unnecessary visits, limiting the collection of data to what is relevant, monitoring of case report form data by well trained internal auditors versed in GCP. It was recommended that a GAVI Task Force on Research and Development should convene experienced public sector investigators, representatives of regulatory agencies, and heads of departments of clinical research from industry to formalize agreement on ways to simplify and economize clinical trials.

Global infrastructure for vaccine trials. Several examples were given of facilities, sites and networks with clinical trials capability in both industrialized and developing countries. The NIAID, NIH, supports a range of clinical trial networks including those devoted to refinement of phase I products as well as those capable of doing Phase III efficacy trials. The system is flexible and allows subcontracting to sites with specific populations. In addition to these vaccine evaluation units, NIAID supports the development of several clinical sites in developing countries,

although the clinical emphasis is primarily on HIV and malaria. The United States DOD has unique clinical trial sites within the DOD setting that allows for clinical capacity that includes sporozoite challenge for malaria vaccine candidates. DOD also supports several foreign sites in Asia, Africa and Latin America.

The European Commission assumes no direct responsibility for clinical trial infrastructures in Europe. However, being a major sponsor of vaccine research in Europe, there is a strong interest in this issue, and broad-based consultations on European Union-wide vaccine research and development capabilities have identified a need to strengthen vaccine trial infrastructure. Existing infrastructures, which are mostly designed for research on specific vaccines and located in countries with long-standing tradition in vaccine development, include a few large centres such as the Oxford Vaccine Group. A recent initiative in Germany is calling for the establishment of a new centre of competence in vaccine research. Enhanced coordination among the various established and emerging European efforts is desirable.

Mahidol University established a vaccine trial centre (VTC) in 1986. During the past 13 years, the VTC, which has both inpatient and outpatient facilities, has gained experience in conducting vaccine trials for at least 10 different vaccines, including challenge studies. Most recently, the Thai HIV/AIDS vaccine trial project has required the development of an infrastructure for consensus building, advocacy and bioethics.

The IVI in Seoul, Korea is focusing on the development of an epidemiological and clinical trial network in Asia. In addition to clinical and biostatistical capability, social and economic modeling capabilities are part of this effort. IVI is currently evaluating their ability to coordinate a multi-country trial focused on disease burden using common protocols and methods.

The Medical Research Council Laboratories, in Fajara, the Gambia, in West Africa, has been a bastion for the evaluation of candidate vaccines in Phase I-III clinical trials. These have included vaccines against hepatitis B, bacterial meningitis and pneumonia, diarrheal disease, and malaria.

In South America, the Centro para Vacunas en Desarrollo, Chile (CVD-Chile) has been a leader for years in the performance of Phase I-IV clinical trials of many vaccines. These have included studies of typhoid, cholera, Hib conjugate, pneumococcal conjugate, and intranasal influenza vaccines, and combination infant vaccines. Follow-up for as long as seven years was maintained in one large-scale trial.

While the global clinical trial capability was found to be generally adequate overall, the absence of developed sites for tuberculosis efficacy studies and the complexity of the study design for those trials was noted.

Overview of sites for clinical trials. Participants in the meeting represent just a fraction of the sites in industrialized and developing countries where the inftastructure and the presence of experienced clinical investigators will allow well executed clinical trials to be carried out under GCP. The conclusion is that the global capacity for performing clinical trials is presently in good shape, although further strengthening of specific sites will be necessary for specific projects. Table 3 summarizes some of the clinical trial sites in industrialized countries that have a track record for

performing clinical trials of developing market vaccines such as those to prevent malaria, dengue, cholera, typhoid, Shigella dysentery and diarrhea due to enterotoxic *Escherichia coli*. Table 4 summarizes sites in Asia, Africa and Latin America that have a similar track record of performing clinical trials of the same vaccines. Table 5 lists a number of sites in Asia and Africa that are being prepared to undertake clinical trials of developing market vaccines. It was deemed important to emphasize that substantial financial and human resources must be committed over the next decade to maintain the viability of the current clinical trials sites and to prepare new sites for specific projects.

GAVI pull strategies for research and development

The Pre-Task Force on Research and Development focused on ways to push the research and development agenda for the development of developing market vaccines. In order to provide a broad picture of the different ways in which GAVI will be attacking the overall problem, several members of the GAVI Task Force on Financing reviewed the ways in which that Task Force is attempting to create pulls, i.e., incentives for industry to invest in research and development for developing market vaccines.

Creating incentives for investment. An impetus for the creation of the GAVI Task Force on Financing was to identify and address the issues of critical importance to industry that influence whether or not they will become involved in the effort to develop vaccines against diseases of primary interest for developing country use. One of the central issues was that of credibility. Specifically, industry related its need to be able to demonstrate that there is a credible market for the new products that it develops.

The failure of countries in the developing world to include yellow fever vaccine and hepatitis B vaccines in their national immunization programmes, despite WHO recommendations and the low and high cost–benefit ratio for these vaccines, indicates that considerable education and advocacy remains to be done.

Five key items were identified that are essential in creating the industrial incentive for future investment. These include:

- Stimulating national demand;
- Developing guarantee purchase mechanisms;
- Providing realistic forecast of vaccine use;
- Protecting intellectual property rights; and
- Increasing government ownership/responsibility for national immunization systems, including the introduction of new vaccines.

Affirming this viewpoint, the industry representatives at the meeting emphasized that it is the likelihood for a satisfactory return on investment that is the most fundamental concern for industry. Five items were identified as factors that could pull industry into this arena. They were summarized as real corporate motivation and include:

- Availability of infrastructure for vaccine distribution;
- Advocacy for the vaccine, specifically consensus about the desirability of a product;
- Demonstration that developing countries are credible and sustainable markets for new products;
- Vaccine prices in these that provide a reasonable margin of profit.

It was the general view of the Pre-Task Force participants that programmatic implementation of Hib and HBV more widely in developing countries will be crucial for establishing credibility for the involvement of industry in participating in research and development for vaccines against parasitic diseases, diarrheal diseases, and other priority diseases.

What role does intellectual property play in research and development for developing market vaccines?

Protection of intellectual property through patents is an important incentive to industry, as it assures that their investment will be protected for a number of years, once a vaccine reaches licensure and can be commercialized. Thus, strong intellectual property positions stimulate the vaccine development process and and can hasten its pace. Equally important to intellectual property, is the credibility of the licensee. However, the most critical issue of all appears to be the marketability of the product.

Difficulty in paying patent costs, especially in purely academic situations, was identified as a barrier. Recognizing that protection of intellectual property through the successful issuance of patents is a key to eventually being able to attract industrial partners, the high costs of filing and maintaining patents for academic investigators in industrialized as well as developing countries was pointed out. This is a fundamental problem that must be solved. If not, many of the basic research discoveries made in academic institutions that can form the basis of constructing vaccine candidate against diseases of importance to the developing world will not be protected and, therefore, will not be of interest to future industrial partners. Two possible options were proposed. The first, is to try to partner early with industry so that the industrial partner will absorb these costs. In fact, in the current reality, this is unlikely to succeed for the various reasons already cited that explain why major industry has little interest in developing market vaccines. At present there is no rationale for industry to pay the patent filing costs for vaccines in which they have little interest in investing. The second option is more realistic and could constitute an important contribution by GAVI. When no industrial sponsor comes forth, a request could be made for GAVI to pay the patenting costs, perhaps through the R & D Window of GAVI's Global Fund for Childrens Vaccines; in exchange, royalties from the ultimate sales of the vaccine could go back into the Fund. In this way, several hurdles would be overcome: 1) Intellectual property would be protected by acquisition of patents so that at a later point, if the discovery matures into a vaccine candidate, it may be possible to attract an industrial partner; 2) this may help a vaccine against a disease of primary interest to developing countries to be developed to the point of licensure; 3) assuming that other segments of GAVI successfully create guaranteed markets for the use of this vaccine, a proportion of the royalties from sales of the vaccine would be returned to the GAVI Fund to be used for other patent filings. Obviously, many specifics of such an approach would have to be worked out

and this would have to be limited to the specific vaccines that are highest on GAVI and development.

Another instance in which intellectual property impacts on vaccine development is when there exist different owners of distinct intellectual properties, all of which may be required to create the most scientifically rational vaccine. This is a complex issue. Ideally, in view of the global public health imperative for the vaccine, GAVI could somehow foster an accommodation among the parties that would allow rational vaccine development research to proceed.

Coordination of global efforts

The participants concluded that a GAVI Task Force on Research and Development should respect the energy, ingenuity and innovation of the various existing independent projects, programmes and research groups globally that are working to develop vaccines to prevent the diseases of developing countries. On the other hand, because resources are limited and the global needs are many, participants argued that a Task Force that can enhance communication among disparate groups in the research community, convey global priorities, establish liaisons and collaborations (between North and South, bench and clinical, public sector and private industry), solve certain generic problems (e.g., access to pilot lots; simplification of clinical trials) and provide global leadership, would be an important step forward.

Summary: strengths, gaps and items for action

- GAVI should foster research and development of developing market vaccines against diseases for which the burden is largely limited to the developing countries.
- A Task Force on Research and Development should be established to join the other three Task Forces that assist the GAVI Secretariat and Working Group to achieve GAVI's objectives.
- The GAVI Task Force on Research and Development should work with WHO, epidemiologists from developing countries, industry, UNICEF, World Bank and other partners to set the priorities for which developing market vaccines, in addition to HIV, malaria and tuberculosis, are most needed.
- Where epidemiologic, microbiologic or parasitologic data are deemed to be insufficient to allow a fair assessment of disease burden, the collection of those data should be undertaken.
- A GAVI Task Force on Research and Development should "push" the development of these vaccines by:
  - fostering partnerships with industry;
  - assisting in obtaining patent protection;
  - providing access to pilot lot formulations (through various mechanisms);
  - facilitating sponsorship (i.e., financial support) for clinical trials;
  - exploring ways to make clinical trials simpler and more economical.

- The global capacity for production of pilot lot formulations of different types of vaccine under GLP and GMP should be catalogued (and periodically up-dated).
- The GAVI Task Force on Research and Development should, in collaboration with DMID, NIAID, review future annual issues of the Jordan Report prior to publication to ensure that progress on research on the GAVI priority vaccines is contained therein.
- The GAVI Task Force on Research and Development should oversee the preparation of a catalogue of clinical trials facilities in industrialized and developing countries with experience or potential for evaluating developing market vaccines in Phase 1–IV clinical trials. (This must be annually up-dated).
- GAVI should foster the viability of the clinical trials research units in Africa, Asia, and Latin America, that have established track records in performing GCP clinical trials in adult and pediatric populations.
- Non-profit companies and "virtual corporation" models are attractive strategies to be pursued for nurturing the development of certain developing market vaccines.
- More direct forms of academia/industry partnership should also be encouraged.
- The GAVI Task Force on Research and Development should actively explore opportunities in large developing countries such as Brazil, China, India and Indonesia that have large-scale manufacturing capacity and strong research capability.
- The "push" activities of the GAVI Task Force on Research and Development should be coordinated with the "pull" efforts of the GAVI Task Force on Financing to achieve synergy.

Table 1: Results of a highly informal, preliminary survey among meeting participants to ascertain the priority ranking of developing market diseases that should be targeted for accelerated research and development

New vaccines (none currently licenced)	Overall ranking
Shigella	1 (73)
Dengue	2 (66)
ETEC	5 (49)
Schistosomiasis	7 (24)
Leishmania	8 (21)
Hepatitis C/E	9 (17)
Improved vaccines (licenced vaccines exist)	**Overall ranking**
Typhoid	3 (56)
Group A meningococcus	3 (56)
Japanese encephalitis	6 (42)

(Counting: first rank = 4 points, second rank = 3 points etc) This is a ranking of 29 responses. Respondents identified their areas of expertise as including, basic vaccine development, clinical vaccinology, immunology, industrial vaccine development, microbiology, public health, epidemiology, parasitology, regulatory affairs and jurisprudence.

Table 2: Sensitivity analysis for the burden of *Shigella* disease in developing countries

Age strata	**0–11 mo**		**1–4 yrs**		**5–14 yrs**		**15–59 yrs**		**>60 yrs**	
Total population	125 000 000		450 000 000		1 011 000 000		2 647 000 000		330 000 000	
DISEASE BURDEN	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
No. diarrhea episodes/person/yr	2.7	5.0	1.7	3.0	0.65	0.65	0.5	0.5	0.69	0.69
Total diarrhea (TD)episodes/yr	337 500 000	625 000 000	765 000 000	1 350 000 000	657 140 250	657 140 000	1 323 304 000	1 323 304 000	227 320 500	227 320 500
Diarrhea episodes in domicile (DD)										
No. episodes (% of TD)	297 675 000 (88)	551 250 000 (88)	703 035 000 (92)	1 240 650 000 (92)	643 997 450 (98)	643 997 450 (98)	1 296 837 920 (98)	1 296 837 920 (98)	222 774 090 (98)	222 774 090 (98)
No. *Shigella* (% of DD)	5 954 000 (2)	27 563 000 (5)	42 182 100 (6)	235 723 500 (19)	6 439 970 (1)	19 319 920 (3)	12 968 380 (1)	38 905 140 (3)	2 227 740 (1)	6 683 220 (3)
Diarrhea episodes in outpatients (OD)										
No. episodes (% of TD)	34 763 000 (10)	64 375 000 (10)	60 435 000 (8)	106 650 000 (8)	13 142 810 (2)	13 142 810 (2)	26 466 080 (2)	26 466 080 (2)	4 546 410 (2)	4 546 410 (2)
No. *Shigella* (% of OD)	695 000 (2)	19 313 000 (30)	7 856 550 (13)	41 593 500 (39)	657 140 (5)	2 759 990 (21)	793 980 (3)	7 145 840 (27)	409 177 (9)	1 545 780 (34)
Diarrhea episodes hospitalized (HD)										
No. of episodes (% of TD)	5 063 000 (2)	9 375 000 (2)	1 530 000 (0.2)	2 700 000 (0.2)						
No. with *Shigella* (% of HD)	203 000 (4)	1 031 000 (11)	122 400 (8)	864 000 (32)						
No. *Shigella* episodes										
Subtotal by age strata	6 852 000	47 907 000	50 161 050	278 181 000	7 097 115	22 079 910	13 762 360	46 050 980	2 636 920	9 774 780
Subtotal by age group		**Low:** 57 012 300	**High:** 326 087 250				**Low:** 23 496 390	**High:** 89 488 332		
Total annual *Shigella* episodes					**Low: 80 508 690**	**High: 415 575 580**				
MORTALITY	**Low**	**High**	*Low*	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Mortality from HD with *Shigella*										
Uncorrected (% of HD)	28 150 (14)	143 340 (14)	11 510 (9)	81 220 (9)	53 890 (8)	226 320 (8)	65 110 (8)	585 960 (8)	33 553 (8)	126 750 (8)
Corrected for out-of-hospital mortality	112 600 (4x)	1 433 440 (10x)	46 020 (4x)	812 160 (10x)	215 540 (4x)	2 263 190 (10x)	260 430 (4x)	5 859 590 (10x)	134 210 (4x)	1 267 540 (10x)
Subtotal by age group		**Low:** 158 610	**High:** 2 245 600					**Low:** 610 180	**High:** 9 390 320	
Total annual *Shigella* deaths					**Low: 768 790**	**High: 11 635 920**				

(From Kotloff et al, Bull WHO 77:651–666, 1999)

Table 3: A partial survey of the public sector clinical trials facilities in industrialized settings that have a track record in evaluating developing market vaccines such as vaccines against malaria, cholera, typhoid fever, *Shigella* dysentery and enterotoxigenic *Escherichia coli* (ETEC) diarrhea and dengue fever

Institution	Location	Phase I	Phase II	Phase IIB (challenge)	Phase III[b]	Phase IV
WRAIR/ NMRI	Silver Spring, Maryland	Malaria *Shigella* ETEC Cholera Dengue	Malaria *Shigella* ETEC Cholera Dengue	Malaria *Shigella* ETEC Cholera	Malaria ETEC Cholera Typhoid	
Center for Vaccine Development, U. of Maryland (NIH VTEU network[c])	Baltimore, MD	Malaria *Shigella* ETEC Cholera Typhoid Dengue	Malaria *Shigella* ETEC Cholera Typhoid Dengue	Malaria *Shigella* ETEC Cholera	Typhoid Cholera *Shigella*	Hib conjugate
U. of Cincinnati (NIH VTEU network)	Cincinnati, Ohio	Cholera	Cholera	Cholera		
Dep't. of Microbiology, Baylor Univ.	Houston, Texas	Malaria	Typhoid			
Dep't. of Med. Microbiology, U. of Goteborg	Goteborg, Sweden	Cholera ETEC	Cholera ETEC		Cholera ETEC	
Karolinska Institute	Stockholm, Sweden	*Shigella* Typhoid	*Shigella* Typhoid			
Queensland Institute of Medical Research	Brisbane, Australia	Malaria	Malaria			
Israel Defense Force	Israel	*Shigella* ETEC	*Shigella* ETEC		*Shigella* ETEC	
St. George's Hospital Medical School	London, UK	Cholera	Cholera			

[a] WRAIR = Walter Reed Army Institute of Research; NAMRI = Naval Medical Research Institute

[b] With the exception of Phase III studies carried out by the Israel Defense Forces, the other Phase III and Phase IV trials performed by the institutions listed in this table were in carried out in collaboration with institutions in developing countries listed in Table 4.

[c] There are several other independent units in the NIH VTEU (Vaccine and Treatment Evaluation Units) network. However, they do not have an established track record of working on developing market vaccines.

Table 4: A partial survey of the public sector clinical and field trial sites in developing countries that have a track record of evaluating developing market vaccines

Institution	Location	Phase I	Phase II	Phase III	Phase IV
Medical Research Council Laboratories	Fajara, The Gambia, West Africa	Malaria HBV Hib conjugate Pneumo conjugate Mening conjugate	Malaria HBV Hib conjugate Pneumo conjugate Mening conjugate	Malaria HBV Hib conjugate Pneumo conjugate	
National Institute for Health Research & Development & NAMRU–3	Jakarta, Indonesia		Cholera Typhoid	Cholera Typhoid	
AFRIMS	Bangkok, Thailand		Japanese B encephalitis Hepatitis A	Japanese B encephalitis Hepatitis A	
NMRI Detachment	Lima, Peru		Cholera	Cholera	
NAMRU–2	Cairo, Egypt	ETEC, Typhoid	ETEC, Typhoid	ETEC, Typhoid	
CVD–Chile conjugate	Santiago,	Cholera Chile Hib conjugate Pneumo conjugate	Cholera Typhoid Hib conjugate Pneumo conjugate Mening. conjugate	Typhoid Typhoid conjugate	Hib Pneumo
Institute of Nutrition	Lima, Peru		Cholera	Cholera	
Inst de Medicina Tropical	Caracas, Venezuela		Malaria	Malaria	
ICDDR,B	Bangladesh	Cholera ETEC *Shigella*	Cholera ETEC *Shigella*	Cholera	
Vaccine Trial Centre, Mahidol University	Bangkok, Thailand	Cholera Dengue	Cholera		
Ifakara Centre & Unidad de Epidemiologia, Hospital Clinic, Barcelona, Spain.	Ifakara, Tanzania.	Malaria	Malaria	Malaria	
Lanzhou Institute of Biological Products	Lanzhou, China	*Shigella* Cholera	*Shigella* Cholera	*Shigella*	
Nat. Inst. of Hygiene & Epidemiology	Hanoi, Vietnam	Cholera Typhoid	Cholera Typhoid	Cholera Typhoid	

NAMRU = U.S. Naval Medical Research Unit; NMRI = U.S. Naval Medical Research Institute; AFRIMS = Armed Forces Medical Research Institute; CVD–Chile = Centro para Vacunas en Desarrollo, Chile; ICDDR,B = International Center for Diarrhoeal Diseases Research, Bangladesh

Table 5: A partial survey of the public sector clinical and field trial sites in developing countries that are being prepared to evaluate developing market vaccines but that have not yet undertaken clinical trials with these vaccines

Institution	Location	Phase I	Phase II	Phase III	Phase IV
Papua New Guinea Institute of Medical Research	Madang, Papua New Guinea	Planned	Planned	Planned	
International Vaccine Institute	Seoul, Korea	Planned	Planned	Planned	
Noguchi Memorial Inst. for Med. Res. & Navrongo Health Research Ctr & NMRI	Navrongo, Ghana	Planned	Planned	Planned	
Centro de Investigaci ó n en Salud de Manhiça & the Unidad de Epidemiología, Hospital Clinic, Barcelona	Manhiça, Mozambique	Planned	Planned	Planned	
CVD, U. of Maryland & U. of Mali Malaria Research & Training Center	Bandiagara, Mopti Region, Mali	Planned	Planned	Planned	

CVD = Center for Vaccine Development

Reproduction of a slide presentation

Task force for research and development

- To foster “developing market” vaccines specifically needed by developing countries
- “Push” mechanisms to complement “pull” strategies
- Identify generic gaps and obstacles
- Public/private collaborations to accelerate pre-clinical and clinical development:
  - With “big pharma”
  - With developing country industry
  - Not for profit “virtual corporations”
- Public sector must disproportionately assume costs of the early high risk steps in vaccine development

GAVI

Task force for research and development

- Preliminary analysis has identified important gaps to be filled and obstacles to be overcome:
  - More precise disease burden data needed
  - Initiate a systematic process for prioritizing needed vaccines other than HIV, malaria & TB
  - Assist academia to file patents (create intellectual property)
  - Provide access to pilot lot formulations
  - More bioengineers skilled in making pilot lots & scale-up
  - Simplify & economize Phase I & II clinical trials
  - Strengthen productive clinical trials sites
  - Initiate some new sites (e.g., for testing TB vaccines)
  - Increase R&D funding to accomplish these tasks

GAVI

Accelerating Vaccine R&D: Market incentives

- Pull strategies -- Growing attention
  - Market failure resulting in under-investment in R&D for global public goods
  - Industry is a pivotal partner: public sector can not do it alone
  - Industry decisions driven by risk - return ratio
  - When there is a failure, the public sector must influence both risk and return through push and pull strategies to provide adequate incentives

GAVI

Accelerating Vaccine R&D: Market incentives

- New players
  - GAVI - Task Force on Financing
  - Commission on Macro-economics and Health
  - Gates Foundation
  - World Bank
  - WHO Round table with Industry
  - Academia (Harvard, USCF)
  - Gates funds recipients (IAVI, MVI, Sequellae)

GAVI

New activities: Coordinating bodies

- GAVI - Task Force on Financing
  - Mandate: Coordinate work of GAVI partners in exploring and developing financing mechanisms or strategies to address under-investment in immunization programs by governments and partners and investment decisions by industry
  - Developed living global workplan of partners work
  - Planned activities include identifying incentives for private companies; maximizing impact of procurement strategies; furthering credibility of market for today's vaccines, exploring broader use of loans/credits.

GAVI

New activities: Coordinating bodies

- WHO Commission on Macro-economics and Health
  - Objective: Coordinate work of partners in examining the economics of incentives for new vaccine and product development in conjunction with other partners
  - Planned activities include identifying priority diseases and products; identifying incentives for private sector commitment and support; engaging in high level consultations and advocacy

GAVI

New activities: Partner support

- Gates Foundation
  - Fund AIDS, malaria and TB vaccine development ($100 million)
  - Through IAVI, MVI, Sequellae - new strategies in IPR agreements for access rather than equity stake, facilitating strategic alliances with developing country partners, high level advocacy
  - Fund GFCV for current “new” vaccines ($750 million)
  - Potential to fund new strategies and purchase of new products

- World Bank
  - Study and high level consultation on incentives to accelerate R&D of AIDS vaccine for developing countries
  - Potential corporate decision to use WB loans/credits to address market failure

GAVI

New activities: Partner support

- WHO Round table with Industry:expand dialogue between WHO and mfgs

- Academia (Harvard, USCF)
  - Coordinating meetings on subject
  - Disseminating information through publications/presentations
  - Exploring theories of pricing, demand/supply

GAVI

Annex 5:

Laying the foundation for global health: a panel session to launch GAVI at the World Economic Forum meeting in Davos

The organizers of the World Economic Forum (WEF) meeting in Davos developed a special panel session "Laying the foundation for global health: the GAVI Initiative", in which the following questions were posed:

- How can business play a role in immunization?
- Who will bear the cost of not acting now?
- Can market incentives spur research into, and action against, diseases which predominantly affect developing countries?

The GAVI session has been featured prominently by the WEF organizers – on the WEF website, during press meetings and a press conference held in Geneva prior to Davos, and during other panel sessions in Davos.

The chair of the GAVI Board of Directors, Gro Harlem Brundtland, Director-General of the World Health Organization, opened the session. Also on the panel were, in speaking order: William H. Gates III, Founder of the Bill and Melinda Gates Foundation; Joaquim Alberto Chissano, President of Mozambique; Carol Bellamy, Executive Director of the United Nations Children's Fund (UNICEF); Raymond V. Gilmartin, Chairman, President and CEO of Merck and Co.; and James D. Wolfensohn, President of the World Bank.

Summary of remarks by Dr Brundtland

The fact that 1.3 billion people around the world live on less than one dollar a day is bad for business; in a globalized world, one region's poverty is another region's opportunity lost. More than anything, poverty means bad health, and bad health means low productivity. Malaria costs at least one per cent of GDP in many African countries through lost productivity. HIV/AIDS is devastating whole economies. Tuberculosis drives millions of families deeper into poverty every year through medical expenses and lost income.

We can turn this around. Improved health means improved productivity. It can be very simple. The most cost-effective health intervention of them all is childhood immunization. For only USD 17 per child, we can provide lifetime protection against the six historical scourges – polio, diphtheria, tuberculosis, pertussis, measles and tetanus.

The Global Alliance for Vaccines and Immunization has been formed to kick-start a campaign to increase vaccination coverage. GAVI is a true partnership between public and private sector. It is one based on enlightened self-interest, but it is also one that recognizes the moral responsibility we all have for a world where all children receive a basic chance of survival and health.

Summary of remarks by Mr Gates

Millions of lives have been saved by the massive efforts to increase immunization in the 1980s. But millions of lives are still being lost because the vaccines that we in the industrialized countries take for granted are not yet available in many of the poorer countries. Typically it has taken 15–20 years from the time a new vaccine is available in the United States and other industrialized countries before it becomes more broadly available. After speaking with scientists and undertaking my own research, it has become clear that it is more important to help the world secure basic health rights than to ensure that every person had access to the Internet.

The critical need to get today's vaccines out to more children and developing new vaccines for diseases such as AIDS, malaria and tuberculosis has had very little visibility until now. There hasn't been the will to take this to the next level. That is why it is so gratifying to see this issue raised in a number of sessions at the World Economic Forum, including this session. Also gratifying is the commitment from President Clinton to ask Congress to provide GAVI with USD 50 million for the Global Children's Vaccine Fund.

We need cooperation from many groups – governments in the developed world, governments in which vaccine coverage is low, and the pharmaceutical industry – in order to make this happen. We are just getting the critical mass and GAVI is galvanizing people to say, yes, we can do better. It is a privilege to be a part of something that is going to have a positive impact on the world's children.

Summary of remarks Mr Chissano

My country was in war for 16 years during which time the population was spread, with many refugees moving into neighbouring countries. As a result, we had a very large period of time when we could not immunize children and adults alike. During this time, new health threats were spreading, such as AIDS. AIDS is such a problem because we have no cure, but in fact it is malaria that is killing more people in our country than any other disease. In addition to these two diseases, there are other major health threats, such as tuberculosis.

The problem is that we don't have the means. We had to rebuild all that was destroyed by war, including health and education facilities. These two are very important for vaccination programmes. The issue of vaccination cannot be seen in isolation. It needs to be seen within the context of all health problems. Resources are so meagre that we need to establish the balance between preventive medicine, and treatments.

Another very important aspect to increasing immunization rates is the development of research capacity in the countries. Research cannot only be conducted in the United States or Japan and then brought to Mozambique or Liberia. The international community, bilateral donors and the private sector need to help establish research

centres and pharmaceutical production facilities close to the people who need the vaccines. In this regard, the transfer of technology will be very important. A new ministry of science and technology has been formed, with the aim of bringing us closer to the technology.

Summary of remarks by Ms Bellamy

As Mr Gates mentioned, in the late 1980s there was huge push for universal vaccination, driven largely by WHO, UNICEF and Rotary International. These efforts were very successful; by 1990 global immunization coverages had reached nearly 80% coverage of all the world's children. But we still are seeing millions of children dying unnecessarily. We have the technology – the vaccines, the safe injection materials – to reduce disease and death among all the world's children. What we need is to work together, to mobilize political will and the financing necessary to bring this about.

GAVI brings together the very important different actors into a broad-based strong alliance, with a strong commitment for financing. But even with the commitment from the Gates Foundation and President Clinton we know that we will need more. In fact, that is a reason why we have come here to the World Economic Forum to speak with you.

The success of the Children's Challenge will depend on a commitment by private and public sector leaders to support the right of every child to vaccination. The same resolve that markets products in poor rural villages and sends television programming into the most remote corners of the world can surely overcome all the usually cited barriers to universal immunization. The use of mass media has been crucial to the success of immunization programmes so far but we've got to explore all possible means from wind-up radios to hand-held cameras.

Summary of remarks by Mr Gilmartin

GAVI can serve as a model for corporate and public cooperation. Merck is committed to developing new vaccines; we do not have scientific discoveries sitting on the shelves for lack of a market. The development of new vaccines and medicines is high on Merck's agenda; Merck is making exciting advances on the creation of an AIDS vaccine. At the same time, however, there needs to be more emphasis on developing better healthcare systems in all countries. The kind of cooperation that GAVI represents will be essential for improving access to better health care and medicines and making vaccines more accessible.

Merck's experience with Mectizan, a medicine that prevents a disease called river blindness, shows that even the simplest pharmaceutical intervention faces tremendous challenges in delivery. Even after Merck decided to donate the medicine free of cost, it took years of collaboration with international partners and developing countries to develop the protocols necessary to deliver the medicine to those who need it. Today, we are seeing the fruit of that collaboration, with millions of people receiving Mectizan every year.

Building infrastructure, improving delivery systems, political will, and sustained commitment to financing can have a tremendous impact on public health in developing countries. Indeed, by improving health infrastructure, this initiative may further stimulate vaccine research and development. But the success of any sustainable health programme starts with the political will and commitment from local governments.

Summary of remarks by Mr Wolfensohn

Health has emerged as the central issue in a country's development. In a survey conducted by the World Bank among 60 000 people living in poverty, it was found that health is the single largest contributor to poverty, and the single most vulnerable aspect. Health lending is such a good investment because of the direct links between health and poverty, and immunization is one of the most cost-effective health interventions.

Increased child survival has been shown to slow down the rate of population growth, as well as increasing school enrolment; education rates are a key determinant of national productivity. In addition, immunization can reduce production losses caused by worker illness, permit use of natural resources inaccessible due to disease, e.g., malaria zones, and safeguard the gains in life expectancy resulting from years of development efforts.

The World Bank is making a strong commitment to reducing poverty through improving health, by increasing health lending and our influence with finance ministers to raise the priority of health in the broader development context, ensuring a strong focus on the poor. We will also strive to correct the market failure resulting in under-investment in priority new products.

GAVI Launch media coverage

The Global Alliance for Vaccines and Immunization's worldwide initiative was officially launched at the World Economic Forum on 31 January. Media coverage was quite extensive and global. Below we have listed – to the best of our knowledge – those media outlets that covered the story. This is by no means a complete listing, as we are still receiving information on resulting coverage.

Print

Financial Times (UK)

- January 31, 2000, "Gates charity makes Dollars 750m donation", David Pilling *(Quotes James Wolfensohn and President Bill Clinton)*
- February 2, 2000, "Discovering medicines for the poor: Global body aims to create incentives for research into vaccines with little commercial appeal", David Pilling *(Quotes James Wolfensohn and Raymond Gilmartin)*
- January 31, 2000, "FT Guide to the Week: Davos and Child Vaccines"

International Herald Tribune

- February 1, 2000, "UN and World Bank join Gates to announce vaccine initiative", Alan Friedman *(Quotes Bill Gates and Gro Harlem Brundtland)*
- January 31, 2000, Opinion; "A good job: get together now to wire the world", Mark Malloch Brown

- January 28, 2000, “Let’s hear everyone and get on with imaginative solutions,” opinion editorial, James D. Wolfensohn
- January 28, 2000, “Much can be done to make a healthier world,” opinion editorial , Tore Godal and Jeffrey D. Sachs

Chicago Tribune (US)

- February 7, 2000, “Vaccination drive; Gates seeks donors to fight childhood diseases worldwide” *(Quotes Bill Gates and Gro Harlem Brundtland)*

The Toronto Star (Canada)

- February 1, 2000, “Vaccination plan needs cash injection”, David Crane *(Quotes Maria Minna and Gro Harlem Bruntland)*
- January 28, 2000, “Lack of vaccines in poor nations linked to profits”, David Crane *(Quotes Gordon Perkins and Bill & Melinda Gates Foundation)*

The Ottawa Citizen (Canada)

- February 1, 2000, “Gates still expansive as philanthropist, corporate planner”, Alexander G. Higgins *(Quotes Bill Gates)*

The London Free Press (UK)

- February 2, 2000, “Bill Gates not avoiding the limelight” *(Quotes Bill Gates)*

Los Angeles Times (US)

- February 2, 2000, “U.S. outlines bold new global economic policy”, James Flanigan *(Quotes James Wolfensohn)*

The Addis Tribune (Ethiopia)

- January 28, 2000, “Worldwide immunization to be launched”, Staff Reporter

New Scientist (UK)

- February 6, 2000, Editorial; “Don’t forget polio”

The Seattle Times (US)

- January 31, 2000, Daily Briefing *(Quotes Bill Gates)*

Die Neue Zuercher Zeitung (NZZ)

- Neue Zuercher Zeitung, February 1, 2000, “Impfungen fuer Kinder der Dritten Welt”

The Lancet (UK)

- January 29, 2000, “WHO assembles leading economists to study poverty reduction and health; news; brief article; statistical data included” , Haroon Ashraf
- February 5, 2000, “Public and private bodies unite to push for global immunisation”, Haroon Ashraf

Financial Mail (South Africa)

- February 4, 2000, “The West is Reawakened”, Ethel Hazelhurst

Die Zeit (Germany)

Die Welt (Germany)

Nihon Keizai Shimbun (Japan)

Sankei Shimbun (Japan)

The Economic Times (India)

The Asian Age (India)

The Times of India

The Hindustan Times (India)

Time Magazine (European edition), photo

Wires

Reuters (English news service)

- January 31, 2000, (Switzerland) "Gates funded vaccine drive woos allies" *(Quotes Bill Gates, Gro Harlem Brundtland and Carol Bellamy)*

Reuters Health

- January 31, 2000, "Private and public sector effort to immunize children launched" By Alan Mozes *(Interview with Carol Bellamy)*

Associated Press

- January 31, 2000, Associated Press, AP Worldstream *(Quotes Bill Gates and Gro Harlem Brundtland)*

Dow Jones International News Service

- January 30, 2000, "Trade Ministers Ponder Post-Seattle Agenda" By Damian Milverton

Xinhua News Service

- February 1, 2000, "WHO Launches Global Vaccination Program for Children" *(Quotes Gro Harlem Brundtland and Bill Gates)*

Agence France Presse

- January 31, 2000 (Switzerland), "Gates gives cash to child vaccine campaign" *(Quotes Bill Gates and Gro Harlem Brundtland)*
- January 31, 2000 (United Nations), "Gates foundation money behind global vaccination campaign" *(Quotes Gro Harlem Brundtland and James Wolfensohn)*

Deutsche Presse-Agentur

- January 31, 2000, "World children's vaccination campaign launched at World Economic Forum" *(Quotes Gro Harlem Brundtland and Bill Gates)*
- January 31, 2000, "Tansania hofft auf Gavi-Hilfe im Kampf gegen toedliche Krankheiten" by Hendrik Groth
- January 31, 2000, "Kampagne Fuer Kinderimpfung – 750 Millionen Dollar von Bill Gates" *(Quotes Carol Bellamy and Bill Gates)*

Inter Press Service

- February 1, 2000, " Campaign targets vaccine preventable child mortality", Mithre J. Sandrasagra *(Quotes by Gro Harlem Brundtland, Carol Bellamy, Jean-Jacques Bertrand and Joaquim Chissano)*

Schweizerische Depeschen Agentur (sda)

- January 31, 2000, (Switzerland) "Kampagne für Kinderimpfung - 750 Millionen Dollar von Bill Gates" *(Quotes by Gro Harlem Brundtland and Bill Gates)*
- January 31, 2000, (Service de base francais) "Forum de Davos Lancement d'une campagne mondiale de vaccination"

- January 31, 2000, (Servizio di base in Italiano) "Forum di Davos: Lanciata campagna mondiale di vaccinazione"
- January 31, 2000, (Service de base francais) "Lancement d'une campagne mondiale de vaccination; Novartis et Roche ne participent pas Encadre/ Developpement"
- January 31, 2000, (Basisdienst Deutsch) "Neufassung WEF Kampagne fuer Kinderimpfung – 750 Millionen Dollar von Bill Gates" *(Quotes Bill Gates and Gro Harlem Brundtland)*

Associated Press (Germany)

- February 1, 2000, "Impfschutz fuer Kinder soll weltweit verbessert werden Zugang zu Impfstoffen in den Entwicklungslaendern verbessern- Gates-Stiftung stellt 1, 46 Milliarden Mark zur Verfuegung"

ANSA (Italy)

- January 31, 2000, (Milan) "Davos, Campagna per Vaccinazione, Gates Da' 1.500 MLD" *(Quotes Bill Gate and Gro Harlem Brundtland)*

Recoletos (Spain)

- February 1, 2000, "Bill Gates Dona 750 Millones de Dolares Para Vacunas" *(Quotes Gro Harlem Brundtland)*

AFX (Swiss)

- January 31, 2000, "Bill Gates wirbt in Davos fur die Kinderimpfung"

U.N. Wire

Broadcast (TV & Radio)

- CNN Insight, January 31, interview with Bill Gates (transcript attached)
- BBC Radio 4, "The Today Programme," Feb. 1, interview with Bill Gates (transcript attached)
- BBC2 TV Newsnight, January 28, interview with Patty Stonesifer (transcript attached)
- BBC Latin American Service
- BBC World Service Radio
- BBC Focus on Africa Radio
- WCBS TV (CBS affiliate, New York)
- Swiss Radio International
- World Radio Geneva
- Radio France International
- National Public Radio
- CBS Radio
- Radio France International
- CBC Radio (French)
- UN Radio (French)
- BBC World Service Radio (French)
- AP Radio
- Deutsche Welle

- VOA Africa Service
- World News for Public Television (in US)
- RAI SAT (Italian national news)

Update On Paris Launch

- *Le Monde* (one page article on Mali with report on the field trip and story on Davos)
- *Le Figaro* (Science and Medecine supplement)
- *Liberation* (two stories on Paris event and Davos)
- *FR 2* (evening news programme, 4-minutes, with reports from Mali)
- *TF 1* (three minutes, with report from Benin)
- *TV 5* (three reports)
- *France Inter and France Info* (radio interviews on issue and announcement)

Angola Coverage

- Radio National Angola
- Radio LAC
- Radio Ecclesia

Web Coverage

Financial Times

- Online Discussion Forum on GAVI, David Pilling moderator

Newsweek.com

- *The Daily Davos*, "A Talk with a Billionaire" and "Three Million a Year, Vaccines Can Make a Difference to a Lot of Children"

BBC Online

- (Nairobi) "Gates boosts Vaccine Programme, Tanzanian children face death from preventable diseases", Martin Dawes
- "Gates Pledges $750m Vaccine Fund; Bill Gates: still the world's richest man"

University Science (http://unisci.com/)

Africa News Service (two stories)

- January 28, 2000, "Africa-at-Large; worldwide immunization to be launched", staff reporter, Addis Tribune (Addis Ababa)
- January 31, 2000 (Tanzania): "New global campaign to revitalise immunisation efforts", UN Integrated Regional Information Network (IRIN) *(Quotes Bill Gates and in-country experts)*
- February 4, 2000, "Gates Foundation to spur fight against diseases" *(Quotes Gro Harlem Brundtland, Joaquim Chissano, Jean-Jacques Bertrand, Carol Bellamy, Klaus Schwab, Minister Maria Minna of Canada, and Dr Els Borsteilers of Netherlands)*
- February 4, 2000, (Ethiopia): "Immunization campaign launched", staff reporter, Addis Tribune (Addis Ababa).

Annex 6:
Report by the WHO Secretariat on GAVI

This annex comprises a document from the World Health Assembly Executive Board's 105th session, held in January 2000: Agenda item 3.5, document reference EB105/43.

Annex 7:
GAVI Secretariat

Brief updated description of posts excluding Executive Secretary as outline in Proto-Board Meeting report endorsed by GAVI Board

Post	Level	Title	Tasks and accountability
GAVI 2	L 6	Deputy Executive Secretary	Assists the Executive Secretary in relation to the Working Group and Task Forces as well as in the management and direction of the GAVI Secretariat and in representing GAVI. Responsible for handling country proposals. Acts on behalf of the Executive Secretary during periods of absence.
GAVI 3	L 5	Senior Operations Officer	Manages the GAVI operational functions (i.e. finance, accounts, personnel, administration, supply, IT), including administration of GAVI Board and other meetings.
GAVI 4	L 4	Communication Officer	Under the general guidance of the Advocacy Task Force and the Executive Secretary, facilitate the development, implementation and monitoring of communication strategies in support of GAVI's mission.
GAVI 5	GS5	Assistant, III	Under the supervision of the Executive Secretary, implement the communication, documentation and internal managerial coordination activities of the GAVI Secretariat and Working Group.
GAVI 6	GS4	Secretary	Under the supervision of the Deputy Executive Secretary, provide secretarial and administrative support to the GAVI Secretariat. To provide administrative support for meetings, briefings and conferences.

Annex 8:
List of participants

Launch of the Global Alliance for Vaccines and Immunization 31 January, 2000, Davos, Switzerland:

Chair

*Dr Gro Harlem Brundtland, Director-General, World Health Organization; and Chair of the GAVI Board, World Health Organization, 20 Avenue Appia CH 1211 Geneva 27, Switzerland
Tel: 41 22 791 2711/2981/2982; Fax 41 22 791
Email: brundtlandg@who.ch

Mr Jonas Store, Executive Director, Director General's Office, World Health Organization 20 Avenue Appia, CH 1211 Geneva 27, Switzerland
Tel: 41 22 791 2714; Fax: 41 22 791 4846
Email: storej@who.ch

Bill and Melinda Gates Children's Vaccine Program (NGO)

*/**Dr Mark Kane, Director, Bill and Melinda Gates Children's Vaccine Program (Programme for Appropriate Technology in Health – PATH), 4 Nickerson Street, Seattle, Washington 98109, USA
Tel: 206 285-3500; Fax: 206 285-6619
Email: mkane@path.org

Developing Countries

*Honourable Dr Lyonpo Sangay Ngedup, Chairman for Council of Ministers and Minister of Health and Education, Ministry of Health and Education, Royal Government of Bhutan, P. O. Box 108, Thimphu, Bhutan
Tel: 975 2 323 825, 325 431; Fax 975 2 323 113, 323 527
Email: Ngedup@druknet.net.bt

*Dr Lomamy Shodu, Director, Family and Child Health Department, Ministry of Health and Child Welfare, Harare, Zimbabwe, Kaguvi Building, Central Avenue, Harare, Zimbabwe
Tel: 263 04 722 697; Cell: 263 11 800 525; Fax: 263 04 794 734
Email: lshodu@healthnet.zw

Foundations

*Dr Tim Evans, Team Director, Health Sciences Division, The Rockefeller Foundation, 420 Fifth Avenue, New York, NY 10018-2702, USA
Tel. 212 869-8500/212 852-8320; Fax: 212-852-8279
Email: tevans@rockfound.org

**Dr Myron (Mike) Levine, Director, Center for Vaccine Development
University of Maryland School of Medicine, HSF-Room 480
685 West Baltimore Street, Baltimore, MD 21201-1509, USA
Tel: 1 410 706 7588; Fax: 1 410 706 6205
Email: mlevine@umppa1.ab.umd.edu

Industry

*Mr Jean-Jacques Bertrand, Director, Chairman and Chief Executive Officer , Aventis Pasteur, Tour Gamma B, 193-197 Rue de Bercy, 75012 Paris, France
Tel. 33 1 5695 4757/8; Fax 33 1 5695 4755
Email: Jean-Jacques.Bertrand@aventis.com

**Dr Thomas Vernon, Executive Director, Medical, Scientific and Public Health Affairs, Merck Vaccine Division, Merck & Co. Inc., P O Box 4, WP37A-301, West Point, PA 19486-0004, USA
Tel. 1 215 652 8664; Fax 1 215 652 8918

Ministries of Health/Technical Agencies of OECD Countries

*Honourable Dr E. Borst-Eilers, Deputy Prime Minister & Minister for Health, Welfare and Sports, Ministry of Health, Welfare and Sports, P. O. Box 20350, 2500 EJ, The Hague, The Netherlands
Tel. 31 70 340 6510; Fax 31 70 340 5210
Email: ga.v.delft@minvws.nl

Mr Jacob Waslander, First Secretary, Permanent Mission of the Kingdom of the Netherlands, 11 Chemin des Anemones, P. O. Box 276, 1219 Châtelaine, Geneva
Tel. 00 41 22 795 1500; Fax 00 41 22 795 1515
Email: mission netherlands@ties.itu.int

Ministries/Agencies of International Coorporation, OECD Countries

*Honourable Maria Minna, Minister for International Co-operation, Canadian International Development Agency, Hull, Quebec, Canada

*Dr Yves Bergevin, Senior Health Specialist, Health and Population Policy Branch, Canadian International Development Agency (CIDA), 200 Promenade du Portage Hull, Quebec K1A 0G4, Canada
Tel: 1 819 997 7870/613 237 8812; Fax: 1 819 997 9049
Email: yves_bergevin@acdi-cida.gc.ca

**Dr Steve Landry, Technical Advisor, Child Survival, Population, Health and Nutrition Center for USAID, 1300 Pennsylvania Ave. NW, Washington, D.C. 20523-3601, USA
Tel. 1 202 712 4808; Fax 1 202 216 3702
Email: slandry@usaid.gov

Research and Development

*Dr John LaMontagne, Deputy Director, National Institute of Allergy and Infectious diseases, National Institute of Health, 31 Center Drive, Bethesda, MD 20892, USA
Tel: 1 301 496 9677; Fax: 1 301 496 4409
Email: jm79q@nih.gov

United Nations Children's Fund

*Ms Carol Bellamy, Executive Director, United Nations Children's Fund, UNICEF House, 3 United Nations Plaza, New York, NY 10017, USA
Tel : 00 1 212 326 7028; Fax 00 1 212 326 7758
Email: cbellamy@unicef.org

*Mr David Alnwick, Chief, Health Section - Programme Division, United Nations Children's Fund, Three United Nations Plaza, New York, NY 10017, USA
Tel: 212-824-6369; Fax: 212-824-6465
Email: dalnwick@unicef.org

**Dr Suomi Sakai, Senior Health Advisor, Immunization Health Section, United Nations Children's Fund, Three United Nations Children Plaza, New York, NY 10017, USA
Tel. 1 212 824 6313; Fax 1 212 824 6464
Email: ssakai@unicef.org

The World Bank,

*Dr James Christopher Lovelace, Director, Health Nutrition and Population, The World Bank, 1818 H. St. NW, Washington, D.C. 20433, USA
Tel: 202- 458-5125/5520; Fax: 202-522-3234/3489
Email: jlovelace@worldbank.org

**Ms Amie Batson, Health Specialist, Health and Development Network, The World Bank, 1818 H Street NW, Washington, D.C. 20433, USA
Tel: 1 202 458 8300; Fax: 1 202 522 3489
Email: abatson@worldbank.org

World Health Organization

*Dr Michael Scholtz, Executive Director, Health Technology and Pharmaceuticals, World Health Organization, 20 Avenue Appia, CH 1211 Geneva 27, Switzerland
Tel: 41 22 791 4798; Fax 41 22 791 4889
Email: scholtzm@who.ch

**Mr Michel Zaffran, Programme Manager, Vaccines and Other Biologicals, World Health Organization, 20 Avenue Appia, CH 1211 Geneva 27, Switzerland
Tel: 41 22 791 4373; Fax: 41 22 791 4193
Email: zaffranm@who.ch

GAVI Secretariat

**Dr Tore Godal , Executive Secretary, Global Alliance for Vaccines and Immunization, UNICEF, Palais des Nations, 5-7 Avenue de la Paix, CH 1211 Geneva 10, Switzerland
Tel: 41 22 909 5020; Fax: 41 22 909 5931
Email: tgodal@unicef.org

* Board Members
** Working Group Members

Document ordering code:
GAVI/00.01

Available in English only

Printed March 2000

For information,
and/or to obtain copies of this document,
please contact:

Global Alliance for Vaccines and Immunization
c/o UNICEF
CH 1211 Geneva 10
Switzerland

Tel: +41-22-909-5019
Fax: +41-22-909-5931
E-mail: gavi@unicef.ch