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Global Alliance for Vaccines and Immunization

Fifth Board Meeting

London
21-22 June 2001

GAVI Global Alliance for Vaccines and Immunization

Executive summary

1. Status report on GAVI

Discussion

- GAVI has achieved great success in its first two years of operation. As the Alliance evolves, it will need to continue to innovate and learn from experience.
- Now that it is in its implementation phase, the Alliance must strive to take immunization toward a broader perspective and interact with all appropriate players in the health field.
- The architecture of GAVI is not always clear. It would be helpful to have a briefing on the roles of the various task forces, the relations between the GAVI and The Vaccine Fund Boards, the GAVI Secretariat and The Vaccine Fund management, the GAVI Working Group and The Vaccine Fund Executive Committee, and the relations between GAVI and the partners themselves.

Decisions

The Board:

1.1 Agreed that the next Board meeting agenda should include presentations and discussions about the various GAVI and Vaccine Fund structures – who is doing what, how the groups work together.

1.2 Requested that an organigram be developed for this exercise.

2. Status report on The Vaccine Fund

Discussion

- It is essential to have a long-term perspective concerning The Vaccine Fund – beyond five years – so that resources are in place to help finance future vaccines, such as pneumococcal conjugate, as they become available.
- The Vaccine Fund must continue to monitor the balance between funding for purchase of vaccines and health services infrastructure. As The Vaccine Fund receives new resources, the highest priority should be to increase support to immunization services in countries. One proposal is to provide countries with more than one year of share payments for each additional child reached. The Vaccine Fund was requested to conduct further calculations to assess financial implications of this strategy.

- Funding for vaccine research and development should come primarily from partners, but resources from a third sub-account of The Vaccine Fund may be appropriate to fill gaps, at some point in the future, in order to support the GAVI priority research and development (R&D) projects[1] .

- Board members emphasized The Vaccine Fund policy not to replace, or displace, funding from other sources. In this regard, it will be useful to scale up activities on a database to analyse resource flows in immunization, as proposed by the Financing Task Force. This work should be linked to ongoing work being done on national health accounts at WHO and the World Bank.

- The Vaccine Fund was requested to present its fund-raising targets and plans to the GAVI Board at its next meeting.

Decisions

The Board:

2.1 Approved a new Vaccine Fund policy[2] in which countries that receive approval for support from either sub-account of The Vaccine Fund are eligible for three years' supply of auto-disable (AD) syringes and safety boxes for all traditional routine EPI vaccines, or the equivalent amount of money for use in improving safety of immunization programmes. Financial implications of this recommendation are estimated to be up to US$ 17 million per year.

2.2 Approved a new Vaccine Fund policy[2] in which countries that receive approval for introduction of new vaccines from The Vaccine Fund, but have >80% DTP3 coverage and are therefore not eligible to receive funding from the immunization services account, are provided a fixed amount of US$ 100,000 to support costs associated with vaccine introduction activities. Financial implications of this recommendation would be approximately US$2 million in total.

2.3 Approved a cap for funding support to the three big countries – China, India and Indonesia – of US$ 40 million each (over five years).

3. Recommendations from the Country Proposal Review, 4th round

Discussion

- The Board voiced its appreciation for the substance and detail of the written documentation provided by the Independent Review Committee and considered therefore that the oral presentation need only be brief.

[1] To focus efforts on three vaccines (*Streptococcus pneumoniae*, rotavirus and *Neisseria meningitides* group A) and up to three technologies (increasing access to immunization and safety of vaccines and vaccination; improving management of immunization services and disease surveillance).

[2] This decision is retroactive: countries that were approved in past rounds may request new support at the time they submit their inception reports.

Decisions

The Board:

3.1 Endorsed all the recommendations of the Independent Review Committee, namely:

- Approval of proposals from:
  Afghanistan and Zimbabwe (for immunization services) and
  Uzbekistan and Viet Nam (for vaccines).

- Approval, with clarifications on specific issues, of proposals from:
  Nigeria and Yemen (for immunization services);
  Albania, Eritrea, Liberia, Tajikistan, and Turkmenistan (for vaccines); and
  Bangladesh and Zambia (for both vaccines and immunization services).

  Upon receipt of satisfactory clarifications from the respective countries, these proposals would be automatically approved.

- Conditional approval of proposals from:
  Bosnia & Herzegovina, Nigeria, and Zimbabwe (for vaccines).

- Request for re-submission of proposals from:
  Djibouti, Eritrea, Sudan (for immunization services);
  Yemen (for vaccines); and
  Togo (for both vaccines and immunization services).

3.2 Requests The Vaccine Fund Board to approve the above recommendations[3] for which financial implications are estimated to be US$ 23 million for the years 2001 and 2002. The five-year commitment is estimated to be in the order of US$196 million, given current vaccine prices and assuming that the countries consistently reach their targets for immunized children.

3.3 Requests The Vaccine Fund Board to increase the commitment to Ghana[4] from US$ 12.5 million to US$ 38 million over a five-year period, in order to cover the increased costs of introducing pentavalent vaccine earlier than originally planned.

4. Update on China, India, Indonesia

Discussion

- The procedure for proposals for the above three large countries – pre-assessment by the Working Group, then review by the Independent Review Committee before being presented to the Board – is acceptable.

Decisions

The Board:

4.1 Confirmed that India will need to demonstrate strong Government commitment to strengthen immunization services and introduce new and under-used vaccines before its proposal can be funded.

[3] The Vaccine Fund Board subsequently met and approved these recommendations.

[4] The Vaccine Fund Board subsequently met and approved this recommendation.

4.2 Urged that efforts to strengthen capacity of the national regulatory authorities in China will need active monitoring, with clear plans and milestones, in conjunction with the country's multi-year plan. Lack of progress could result in a discontinuation of funding.

4.3 Agreed that, if Indonesia's proposal includes a request to The Vaccine Fund for a pre-filled monodose hepB vaccine to increase efficacy of the birth dose, with Indonesia providing the second and third doses, its proposal could be considered.

5. Injection safety and The Vaccine Fund

Discussion

- Improving the safety of immunization programmes is critical to GAVI's mission. Safety deserves special focus in relation to other elements of immunization programmes.
- A long-term communication effort, led by WHO, UNICEF and the GAVI Advocacy Task Force (ATF), will be necessary to increase awareness of the severity of the problem of unsafe practices and to advocate behavior change – both among health providers and recipients.
- The Task Force for Country Coordination should work on new tools to monitor safety. In developing guidelines for the preparation of annual reports and mid-term reviews, safety should be given special emphasis.
- Appropriate disposal of medical waste is an important element of efforts to improve the safety of national immunization programmes and should be based on the principle that the "polluter pays". Further research is necessary to develop environmentally sound, reasonably priced methods for disposing of medical wastes.

Decisions

The Board:

5.1 Agreed that funds for AD syringes should be awarded on the basis of a review of the injection safety plan component of the country's application to GAVI. Countries that have already been approved will be assessed retroactively.

5.2 Requested that the Working Group communicate this new policy to eligible countries and that the ATF consider efforts to gain wider attention for GAVI's commitment to safety.

6. Capacity building

Discussion

- Strengthening capacity of individuals and institutions in countries is critical for the long-term success of GAVI. It would be helpful to have a presentation on the activities and plans of the GAVI task forces and, in particular, the Task Force on Country Coordination (TFCC) at the next Board meeting.
- The framework for strengthening capacity may be too traditional and top-down in its approach. The inter-task force sub-group that has been formed to develop the

framework should strive to seek more creative approaches to ensuring sustainability, including a broader perspective at the country level with an emphasis on the roles of inter-agency coordinating committees (ICCs) and the broader health sector and institutional development.

- It will be important to maintain a focus on capacity building as new mechanisms are developed through the Alliance. One example of this is the immunization data quality audits (DQA) being piloted in countries over the next few months.

Decision

The Board:

6.1 Requested that capacity building be included as a distinct item on the next Board meeting agenda.

7. Countries in complex emergencies

Discussion

The paper presented (Annex 5) was commended for its clarity and breadth of information.

Decision

The Board:

7.1 Agreed to the recommendations in the paper, namely that:

- To ensure sustained funding, GAVI will use its advocacy channels to encourage international and national authorities to include longer-term support to immunization services in their resource mobilization efforts during acute conflict phases.

- In countries with well-functioning national governments and relatively high immunization coverage, there may be vulnerable populations within their borders that are not reached by the health system. GAVI will encourage partners to ensure that immunization services are reaching those at risk.

- In countries where governments are weak or non-functional, GAVI will consider proposals submitted by an operational partner or partners (such as WHO or UNICEF), engaging the multiple partners most suited to reach all parts of the countries (e.g., UNHCR, *Médicins sans Frontières*) with those partners responsible for implementation.

8. Alignment with accelerated disease control initiatives

Discussion

- The Board appreciated the scope of work and insight in the paper presented (Annex 6).

- The issue of reducing childhood mortality from measles, meningitis and other childhood killers is very important to African countries.

- Better integration of disease control initiatives within health systems is crucial. GAVI missed some opportunities in the polio campaign to strengthen capacity for maintaining sustainable services.
- There are many positive lessons to be learnt from the polio eradication initiative on how to reach every child. It is now incumbent upon GAVI to use those lessons to develop systematic outreach strategies in countries with difficult-to-reach populations.
- At this stage in the polio eradication efforts, countries will appreciate a clear statement from GAVI partners that they support eradication. Any efforts to better align immunization efforts must be designed so as not to disrupt or compromise the investments and ongoing efforts in polio eradication.
- Efforts to increase coordination between disease control initiatives will have an impact on the work of all GAVI entities – the Board, Working Group, Secretariat, and task forces. The Advocacy Task Force will need to urgently address issues raised by these efforts.
- In order to ascertain how staff currently funded by the polio eradication initiative should be utilized in the future, it will be important to have an analysis of human resource capacity and shortfalls in countries, including financial implications.
- It is very important for GAVI to cooperate and collaborate with other immunization and health initiatives, but it is equally important for GAVI to maintain its sharp focus and efficient operations. A balance must be found.

Decisions

The Board:

8.1 **Approved** the establishment of a new objective and milestone:

- **Objective**: To support the national and international accelerated disease control targets for vaccine-preventable diseases;
- **Milestone** for the world to be certified polio-free is 2005;

and **requested** that the Working Group consult with partners to identify appropriate disease outcome indicators (polio, measles, maternal and neonatal tetanus [MNT], and vitamin A).

8.2 **Approved** the proposed direction to work towards integration of all immunization initiatives by placing renewed emphasis on GAVI's first objective to "improve access to sustainable immunization services";

In practice this will mean that, as soon as possible and no later than 2003, all annual – subsequent multi-year – work plans for countries should reflect an approach that incorporates routine services, accelerated disease control, introduction of new vaccines, and vitamin A supplementation within the context of the health system. Targets in the national plans would need to match available resources. For this approach to work, all partners at all levels would have to support it technically and financially, especially through their participation in national and regional ICCs and regional working groups;

agreed to consider a revision of all GAVI objectives, milestones, and indicators to support the full implementation of this strategic direction, at an appropriate time in the near future;

requested that, over the next few months, the Working Group further elaborate on the framework for this strategy and its implications for the national work plans and ICCs, and regional and global activities.

8.3 Approved a revision of GAVI objective #2 to read: "Expand the use of all existing safe and cost-effective vaccines, and promote delivery of other appropriate interventions at immunization contacts."[5]

8.4 Recognized the importance of a human resources infrastructure for immunization and requested that UNICEF and WHO develop together, for consideration by the Board, an immunization human resources plan (i.e., minimum staff per country) and costing based on the current human resources, including those that are funded for accelerated disease control (ADC-funded).

9. Update on research and development project agendas and technology transfer

Discussion

- A great deal of progress has been made in moving ahead on the three vaccine projects, but the Board must continue to monitor whether priority vaccines are getting the support necessary to accelerate their development.
- The Board agreed to the substance of the draft statement on technology transfer but felt that the text should be more neutral in tone, and that the new developing-country vaccine manufacturers' network should be consulted in the process.

Decisions

The Board:

9.1 Endorsed the statement that: "Technology transfer must not be treated as an end in and of itself, but should be considered as a means toward GAVI's larger objectives to accelerate the development of priority vaccines and expand the use of all vaccines."

9.2 Accepted the offer of the UK's Department for International Development (DFID) to draft a revised statement on technology transfer.

[5] Prior to this revision, the GAVI objective #2 was to: "Expand the use of all existing safe and cost-effective vaccines."

10. Financing Task Force update, including financial sustainability and user fees

Decisions

The Board:

10.1 Approved the proposed definition of financial sustainability, as follows:

"Although self-sufficiency is the ultimate goal, in the nearer term sustainable financing is the ability of a country to mobilize and efficiently use domestic and supplementary external resources on a reliable basis to achieve target levels of immunization performance."

10.2 Approved a statement to describe the position of GAVI partners on user fees, as follows:

"In the absence of compelling country or regional data unequivocally documenting their value, user fees should not be levied in publicly financed national immunization services."

10.3 Acknowledged the need for continued work to develop a database of immunization financing in countries. This database would include information on immunization funding sources, expenditures and gaps, and would help to guard against replacement funding by The Vaccine Fund. The work plan being proposed by the Financing Task Force (FTF) would require an additional US$ 300,000 over the next six months.

11. Developing-Country Vaccine Manufacturers' Network

Discussion

- The Board welcomed the development of a new network of developing-country vaccine manufacturers, and urged close collaboration between this network and the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).
- The vaccine industry should be viewed as an international industry, and not stratified between manufacturers from developing and industrialized countries. In this context, the Board confirmed the need for an adequate number of active vaccine producers in developing and industrialized countries, maintaining an environment of fair competition while at the same time identifying gaps in research and development.

12. Relationship between the Vaccine Fund and GAVI

Discussion

- While the GAVI Board enthusiastically supported the proposed logo for the Vaccine Fund, it requested that more work be done on the design of a new GAVI logo. Once this is received, the appropriateness of a GAVI logo should be discussed.
- Discussion of the GAVI logo will be via e-mail and/or teleconferences, so that the final decision can be made by the time Children's Summit meets in September. This would coincide with the first meeting of the new Vaccine Fund Board in New York.

- Systems to increase links between GAVI and The Vaccine Fund – especially between the two Boards, the GAVI Secretariat and Fund management, the GAVI Working Group and Fund Executive Committee – must be further developed.
- The linked but distinct roles of GAVI and The Vaccine Fund would be better understood if the role of GAVI that is not directly related to the Vaccine Fund could be more clearly defined.

Decisions

The Board:

12.1 Endorsed the name change of the Global Fund for Children's Vaccines to "The Vaccine Fund" and endorsed the new Vaccine Fund logo selected by the Fund Board.

12.2 Endorsed the recommendation that GAVI and the Vaccine Fund have separate but mutually reinforcing logos and graphic identities, and that language be used to convey the relationship; for example "GAVI: partnering with The Vaccine Fund".

12.3 Recommended that the outcome of the branding study on GAVI and The Vaccine Fund be rapidly disseminated to the different levels of the GAVI partners in order to promote consistent messages throughout the GAVI network.

12.4 Endorsed the idea of increased linkages through common supervision of the GAVI Secretariat and Fund management by the Working Group and the Executive Committee of The Vaccine Fund.

12.5 Requested that the relationships among the partners in the Alliance be further explored and discussed, especially in regard to the two Boards.

13. The Global AIDS and Health Fund

Discussion

- The Board supports the creation of a Global AIDS and Health Fund that is both additional and complementary to existing development assistance.
- Donors recognize the importance of GAVI. The two Funds should not be seen as either/or prospects for funding but as complementary efforts that both require support to address critical health needs.

Decision

The Board:

13.1 Recognized that the GAVI experience and lessons learned could prove helpful to the Global AIDS and Health Fund developers. The Executive Secretary may therefore assist them, if requested.

14. Selection of new GAVI Board members

Decisions

The Board:

14.1 Welcomed the suggestion that the UN Foundation, represented by President Tim Wirth, replace the Rockefeller Foundation on the Board.

14.2 Selected the Pasteur Institute, represented by its General Director Philippe Kourilsky, to fill the Research Institute seat formerly held by the US National Institutes of Health (NIH)[6] .

15. Next GAVI Board meeting

The next meeting of the GAVI Board will be in Ottawa on 17 October 2001, to be hosted by Canada. In addition, Canada will invite participants to a dinner the evening before the meeting, on 16 October 2001.

[6] The three nominations considered for the seat were the Max Planck Institute, the South African Medical Research Council, and the Pasteur Institute.

Agenda

The meeting was preceded by a dinner on 20 June 2001, hosted by the Rt. Honourable Clare Short, the UK Secretary of State for International Development. Ms Short also opened the meeting the following day.

Dr Gro Harlem Brundtland, GAVI Board Chair, gave the keynote address at the dinner.

1. Status report: GAVI – including capacity building and immunization coverage audit)
   (Dr Tore Godal, GAVI Secretariat)
2. Status report: The Vaccine Fund
   (Mr Jacques-François Martin, The Vaccine Fund)
3. Update: China, India, Indonesia
   (Dr Mark Kane, Bill and Melinda Gates Children's Vaccine Program, USA)
4. Project agenda update, including technology transfer policy
   (Dr Myron M. Levine, Director, University of Maryland School of Medicine, USA)
5. Developing-country vaccine manufacturer network
   (Dr Luis Saturnino Herrera Martinez, Center for Genetic Engineering and Biotechnology [CIGB], Cuba)
6. GAVI and the Global AIDS and Health Fund: update:
   - Evolution to date
     (Dr Julian Lob-Levyt, Department for International Development, UK)
   - Next steps
     (Dr David Nabarro, World Health Organization)
   - Relationship between GAVI and the Global Fund for AIDS and Health
     (Mr James Christopher Lovelace, The World Bank)
7. Recommendations from the fourth review of country proposals
   (Ms Caroline Akim, Ministry of Health, Tanzania)
8. Policy issues – complex emergencies, countries over 80%
   (Mr Bo Stenson, GAVI Secretariat)
9. Presentation on branding GAVI and The Vaccine Fund
   (Muse Consulting, USA)

10. Alignment with accelerated disease control initiatives:

    - Introduction
      (Dr Mark Kane, Bill and Melinda Gates Children's Vaccine Program, USA)

    - Analysis and recommendations
      (Ms Tracey Goodman, World Health Organization)
      (Dr Jon Andrus, Global Forum for Health Research, USA)

11. Injection safety and The Vaccine Fund
    (Dr Steve Landry, USAID)

12. Financial sustainability, including Financing Task Force update, user-fee policy
    (Ms Amie Batson, The World Bank)

13. Setting priorities for GAVI and The Vaccine Fund
    (Dr Tore Godal, GAVI Secretariat)
    (Mr Jacques-François Martin, The Vaccine Fund)

14. Other business: selection of new GAVI Board members
    (Dr Tore Godal, GAVI Secretariat)

15. Decision on time and place of next meeting

List of annexes

Annex 1
Status report of the Vaccine Fund

The following spreadsheet was compiled as reference material for the Board's consideration of proposals to fulfil and, perhaps, expand the current mandate of work financed through The Vaccine Fund.

The estimates provide guidance for the GAVI Board's recommendations on the use of current and pending Vaccine Fund resources, as well as the requirements for projected resources to fund potential future commitments. These estimates also show Vaccine Fund staff the magnitude of fund-raising task they face.

The estimates are broken into three sections:

- Existing commitments as determined by current GAVI policy;
- Recommended commitments being proposed to the Board at this meeting;
- Optional commitments to consider – pending additional resources to the Fund.

In each case, the data are broken into individual years as well as cumulative sub-totals for the periods 2000-2005 and 2006-2010.

Estimated existing, recommended, and optional financial commitments - The Vaccine Fund
June, 2001

Note: Italics indicate items estimated from partial or preliminary data. See comments.

US $ millions

Item	2000	2001	2002	2003	2004	2005	Sub-total 2000-05	2006	2007	2008	2009	2010	Sub-total 2006-10	Total 2000-10	Comments
1. EXISTING commitments for 71 countries															
1a. Shares		49	68	54	46	40	257							**257**	Share estimates are US$ 70 million higher than previously to better reflect current plans where countries which begin below 80% are eligible to continue receiving rewards when they move above 80%, instead of stopping the rewards at 80%.
1b. Vaccines & syringes for new vaccines		81	91	126	175	200	673	*135*	*68*	*34*			237	**910**	2001-2003 estimates from UNICEF Procurement; 2004-05 moderate-to-high model projections; 2006-08 decreasing 1/2 of average annual spending while phasing out. 2008 may include countries which begin vaccine in 2002 and phase out to the maximum of 7 years.
Section 1 Total	**-**	130	159	180	221	240	**930**	135	68	34	-	-	**237**	**1,167**	

Item	2000	2001	2002	2003	2004	2005	Sub-total 2000-05	2006	2007	2008	2009	2010	Sub-total 2006-10	Total 2000-10	Comments
2. RECOMMENDED commitments															
2a.China/India/Indonesia															
i) Total commitment (vaccines, syringes, and system strengthening)		10	25	25	25	25	110	10					10	**120**	Actual commitments to each of China, India, and Indonesia, up to a combined maximum of US$120 million, will be determined through country applications.
2b.Improve injection safety of EPI															
i) 71 Fund-eligible countries				17	17	17	51							**51**	Assumes 3 years support if all countries shift to 100% AD syringes. Actual money would flow at different times to meet country needs.
Section 2 Total	-	*10*	*42*	*42*	*42*	*25*	***161***							**171**	
Sections 1 + 2: Total EXISTING and RECOMMENDED commitments															
	-	**140**	**201**	**222**	**263**	**265**	**1,091**	**135**	**68**	**34**	**-**	**-**	**237**	**1,338**	

Note: Italics indicate items estimated from partial or preliminary data. See comments.

US $ millions

Item	2001	2002	2003	2004	2005	Sub-total 2000-05	2006	2007	2008	2009	2010	Sub-total 2006-10	Total 2000-10	Comments
3. OPTIONAL commitments														
3a. Options to increase share commitments from Infrastructure Account (may want to consider ONE of the following options or a blend: increasing share value and length of commitment)														
Current system (US$20/share)	49	68	54	46	40	257						-	**257**	
(i) IF increase share (to US$25)	61	84	67	58	50	321						-	**321**	Estimate if share value increased to US$25/additional child immunized.
(ii) IF 1 additional year (US$20)	*49*	*117*	*122*	*100*	*87*	*474*	*40*	-	-			*40*	***515***	Example: Additional kids reached in 2002 are rewarded in 2002 and 2003. US$20/additional child reached.
(iii) IF 2 additional years (US$20)	*49*	*117*	*171*	*168*	*141*	*645*	*87*	*40*	-			*127*	***772***	Example: Additional kids reached in 2002 are rewarded in 2002, 2003, and 2004. US$20/additional child reached.
(iv) IF 3 additional years (US$20)	*49*	*117*	*171*	*217*	*208*	*761*	*141*	*87*	*40*			*268*	***1,029***	Example: Additional kids reached in 2002 are rewarded in 2002, 2003, 2004, and 2005. US$20/additional child reached.

Item	2000	2001	2002	2003	2004	2005	Sub-total 2000-05	2006	2007	2008	2009	2010	Sub-total 2006-10	Total 2000-10	Comments
3b - d: Considerations for potential purchase of future vaccines															
3b. Future meningococcal A/C conjugate vaccine															
(i) Vaccine for EPI				*4*	*7*	*26*	*37*	*26*	*26*	*26*			*78*	***115***	Assumes cost of US$3.50 per fully vaccinated child, including syringe and wastage. Phasing in 1 million children in mening. belt in 2003; 2 million in 2004; and up to 7.5 million in 2005. Doesn't include catch-up or outbreak control.
3c. Future rotavirus vaccine															
(I)Vaccine for EPI										*260*	*520*	*780*	*1,560*	***1,560***	Assumes cost of US$10 per child, including wastage; Target = 78 million receiving DTP3 in 2005 (37 million in 71 poorest and 41 million in China/India/ Indonesia) phased in over 3 years. 2011 forward estimated at US$ 780 million per year.
3d. Future pneumococcal vaccine															
(I) Vaccine for EPI										*780*	*1,560*	*2,340*	*4,680*	***4,680***	Assumes cost of US$ 10 per dose x 3 doses per child, including wastage; Target = 78 million receiving DTP3 in 2005 (37 million in 71 poorest and 41 million in China/India Indonesia) phased in over 3 years. 2011 forward estimated at US$ 2,340 million per year.
Section 3b-d Total	-	-	-	4	7	26	**37**	26	26	1,066	2,080	3,120	**6,318**	**6,355**	

Annex 2
Review of country proposals, 4th round

Annex 2.1
Summary of the process

The Independent Review Committee met in Geneva from 24 May to 1 June 2001. The Review Committee consisted of eight members – a previous member having left and two new members included (see Annex 2.6). Committee members who had been involved in countries that presented proposals were not present during the deliberations on those countries, and did not take part in the respective decisions, as noted in Annex 2.6 to this Annex.

The Committee considered new proposals from eight countries, re-submissions from six and replies to previous conditional approvals from three. Taking into account that countries can request support from either or both sub-accounts, there was a total of 24 requests: 10 for immunization services support and 14 for new and under-used vaccines support. Out of these 24 requests:

- 4 countries are recommended for approval and 11 for approval with clarifications;
- 3 countries are recommended for conditional approval, and will have to satisfy the conditions in a subsequent review.
- 5 countries' proposals could not be recommended for approval at this stage; these countries will have to re-submit a proposal for a subsequent review.

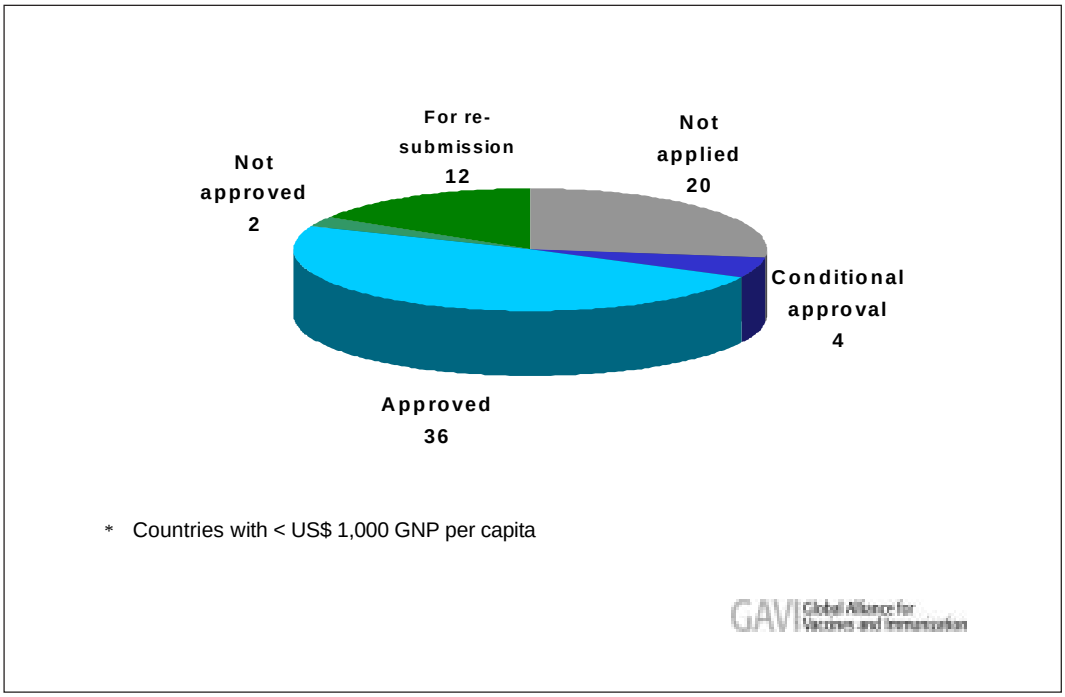
The recommendations from the Review Committee are summarized in Table 1. The financial implications for 2001 and 2002 resulting from these recommendations are estimated to be US$ 23 million (Tables 2 and 3). The five-year commitment is estimated to be in the order of US$ 196 million – given current vaccine prices and assuming that theapproved countries consistently reach their targets for immunized children.

Including the above proposals recommended for support, a total of 36 countries have been approved to receive support from the Fund to date. An additional 16 countries have applied for support, of which 4 have received conditional approval and 12 have been or will be asked to re-submit their proposals (Figure 1).

The overall ratio of recommended approvals and approvals with clarifications to the number of requests is 62%. This is considerably higher than in previous rounds, especially the third round. The Committee considers this to be a reflection of countries' greater awareness of the requirements, and intensified technical support by the partners. The assessment of proposals against GAVI criteria has been consistent and strict.

In order to make it possible, after the third round, to provide the first choice vaccine presentation to a maximum number of countries, two countries – Ghana and Uganda – have been asked to consider if they would be prepared to receive pentavalent (DTP-hepB-Hib) vaccine instead of the previously requested vaccine – tetravalent (DTP-hepB). To date, Ghana has responded positively. This implies an increase in the Fund commitment for new vaccines to Ghana from US$ 12.5 million to US$ 38 million over a five-year period.

Figure 1: Status of 74 countries eligible* for support from GAVI and the Vaccine Fund



Summary recommendations

The Independent Review Committee recommends that the Boards of GAVI and the Fund approve proposals as presented in Table 1, as follows:

- Approval of proposals from Afghanistan, Uzbekistan, Viet Nam, and Zimbabwe.
- Approval with clarifications of proposals from Albania, Bangladesh, Eritrea, Liberia, Nigeria, Tajikistan, Turkmenistan, Yemen, and Zambia. These proposals will be finally approved after satisfactory clarifications are presented.
- Conditional approvals for proposals from Bosnia & Herzegovina, Nigeria, and Zimbabwe.
- Re-submission for proposals from Djibouti, Eritrea, Sudan, Togo, and Yemen.
- Approval of the increased commitment for Ghana as proposed above.

Table 1: Summary of Review Committee recommendations, 4th round

Country	DTP3 coverage 2000	Immunization services	New and under-used vaccines
New proposals, including re-submissions			
Afghanistan	31%	Approval	-
Bangladesh	67%	Approval with clarification	hepB: Approval with clarification
Bosnia & Herzegovina	89%	-	hepB: Contional approval
Djibouti	46%	Re-submission	-
Eritrea	n/a	Re-submission	hepB: Approval with clarification
Liberia	50%	-	YF: Approval with clarification
Nigeria	38%	Approval with clarification	hepB: Not eligible YF: Conditional approval
Sudan	n/a	Re-submission	-
Togo	50%	Re-submission	hepB, Hib, YF; Re-submission
Turkmenistan	99%	-	hepB: Approval with clarification
Uzbekistan	97%	-	hepB: Approval
Yemen	n/a	Approval with clarification	hepB, Hib: Re-submission
Zambia	75%	Approval with clarification	hepB, Hib: Approval with clarification
Zimbabwe	76%	Approval	hepB, Hib: Conditional approval
Conditional approvals from previous rounds			
Albania	97% (1999)	-	hepB: Approval with clarification
Tajikistan	65% (1999)	-	hepB: Approval with clarification
Viet Nam	93% (1999)	-	hepB: Approval

Table 2: Financial commitments 2001-2002, countries recommended for approval

	Immunization services		New and under-used vaccines	
Countries	**3rd quarter 2001: first instalment [1]**	**2nd half 2002: second instalment**	**For 2001**	**For 2002**
1. Afghanistan	519,500	519,500	-	-
2. Uzbekistan	-	-	573,000	973,000
3. Viet Nam	-	-	-	2,375,000
4. Zimbabwe	318,000	318,000	Conditional approval	
Sub-total (US$)	**837,500**	**837,500**	**573,000**	**3,348,000**
Grand total (US$)				**5,596,000**

[1] The calculation of funds for investment is based on targets for the period ending December 2002; it is divided into two equal instalments: the first in July 2001 and the second in July 2002.

Table 3: Financial commitments 2001-2002, countries recommended for approval with clarification (amounts in US dollars)

Immunization services		**New and under-used vaccines**		
Countries	**3rd quarter 2001: 1st instalment[1]**	**2nd half 2002: 2nd instalment**	**For 2001**	**For 2002**
1. Albania	-	-	45,000	121,000
2. Bangladesh	1,785,000	1,785,000	-	388,000
3. Eritrea	*For re-submission*	-	561,000	
4. Liberia	*Approved in November 2000*	41,000	78,000	
5. Nigeria	4,712,000	4,712,000	*Conditional for yellow fever*	
6. Tajikistan	-	-	139,000	174,000
7. Turkmenistan	-	-	94,000	200,000
8. Yemen	283,500	283,500	*For re-submission*	
9. Zambia	169,500	169,500	-1,626,000	
Sub-total (US$)	**6,950,000**	**6,950,000**	**319,000**	**3,148,000**
Grand total (US$)				**17,367,000**

[1] The calculation of funds for investment is based on targets for the period ending December 2002; it is divided into two equal instalments: the first in July 2001 and the second in July 2002.

Annex 2.2
Recommendations for approval, by country
(in alphabetical order)

1. AFGHANISTAN *(New application)*

Immunization services sub-account: Approval

Based upon the targeted number – 103,902 – of additional children to be immunized by 2002, the investment support has been calculated to be US$ 1,039,000; for disbursement in two equal instalments.

2. UZBEKISTAN *(Re-submission from second round)*

New and under-used vaccines sub-account, hepB: Approval

Based upon the request, Uzbekistan will receive hepB monovalent (10-dose vials) vaccine, starting July 2001.

Requirements

	2001	2002
Number of doses (10-dose vials)	1,285,000	2,303,000
AD syringes	1,338,000	2,131,000
Safety boxes	14,870	23,680

Estimated value in US$: 1,546,000

3. VIET NAM *(Conditional from second round)*

New and under-used vaccines sub-account, hepB: Approval

Based upon the request, Viet Nam will receive hepB vaccine starting January 2002:

- HepB monvalent in Uniject[1]:

  Number of doses: 806,000

[1] UNICEF Supply Division expects Uniject to be available from mid-2002 (this will be confirmed by UNICEF at the end of 2001).

Viet Nam *(continued)*

- HepB monovalent (2-dose vials)

Requirements	2002
Number of doses	2,042,000
AD syringes	2,127,000
Safety boxes	23,640
Estimated value in US$:	2,375,000

4. ZIMBABWE *(Re-submission from third round)*

Immunization services sub-account: Approval

Based upon the targeted number – 63,654 – of additional children to be immunized by 2002, the investment support has been calculated to be US$ 636,000; for disbursement in two equal instalments.

Annex 2.3
Recommendations for approval with clarifications, by country

(in alphabetical order)

1. ALBANIA *(Conditional approval from second round)*

New and under-used vaccines sub-account, hepB: Approval with clarifications

Clarifications required:

- Provide annual financial figures in 2001-2005 (Table 2 in Annex 1 of the application form may be used for this purpose).
- Indicate that support from the Fund will not replace current sources of funding for immunization.

2. BANGLADESH *(New application)*

Immunizations services sub-account: Approval with clarification

Clarification required:

- Strategies to mitigate the effects of the phasing-out of outreach sites on immunization coverage and wastage rates.

New and under-used vaccines sub-account, hepB: Approval with clarifications

Clarifications required:

- Provide a plan on the disposal of sharps waste.

3. ERITREA *(New application)*

New and under-used vaccines sub-account, hepB: Approval with clarifications

Clarifications required:

- Provide strategic directions on resource mobilization.
- Provide targets for immunization coverage and vaccine wastage rate, and plans for vaccine waste reduction.
- Recalculate AD syringe requirements in 2002, including buffer stocks.

4. LIBERIA *(New application)*

New and under-used vaccines sub-account, yellow fever: Approval with clarifications

Clarifications required:

- Realistic target to be achieved for YF coverage at the end of five years,
- Rationale/substantiation on proposed target for YF wastage rate (in relation to current measles vaccine wastage rate, which is not provided).
- Re-calculate births, based on an agreed population and realistic birth rate.

5. NIGERIA *(New application)*

Immunization services sub-account: Approval with clarifications

Clarifications required:

- Provide more achievable targets in relation to immunization coverage, number of children to be immunized, and describe strategies proposed to achieve these targets.

6. TAJIKISTAN *(Conditional approval from third round)*

New and under-used vaccines sub-account, hepB: Approval with clarifications

Clarifications required:

- Re-calculate all figures in Tables 4 and 5[1]. A table (attached as Appendix C)[1] was prepared during a GAVI pre-assessment using MOH data from Tables 4.1 and 5. The MOH is encouraged to make use of the attached table to re-calculate targets of children to be immunized with hepatitis B3 vaccine. This will help to determine the required vaccine, syringes and safety boxes in Table 5.
- Provide separate re-calculations in Table 5.1 (for hepatitis B vaccine in one-dose vials) and Table 5.2 (for hepatitis B vaccine in 10-dose vials), taking into consideration the estimated numbers of children to be immunized with each presentation and the respective wastage rates.

The Review Committee noted with concern that the submitted documentation did not include reports on social mobilization preparations for hepatitis B vaccine introduction, nor calculations of additional cold chain storage volume which may be required. The Review Committee requests that Tajikistan report on this in their Inception Report at the end of 2001.

[1] Included in the documentation submitted as part of the Tajikistan request.

7. TURKMENISTAN *(Re-submission from third round)*	
New and under-used vaccines sub-account, hepB:	Approval with clarification

Clarification required:

- Ensure that hepB vaccine, if procured by the country, meets WHO standards.

8. YEMEN *(Re-submission from first round)*	
Immunization services sub-account:	Approval with clarifications

Clarifications required:

- Indicate progress made in expansion of ICC membership, participation, and technical support by partners
- Indicate progress made on the implementation of recommendations from the injection safety assessments and provide plans for reduction of vaccine wastage
- Indicate titles of line items, budget and expenditure for 2000 and 2001 in Annex 1 of the application form.

9. ZAMBIA *(Re-submission from second round)*	
Immunization services sub-account:	Approval with clarifications
New and under-used vaccines sub-account, DTP-hepB-Hib:	Approval with clarifications

Clarifications required on:

- the number of surviving children;
- drop-out rate;
- target numbers of children for immunization;
- update Table 4.1[2].

[2] Included in the documentation submitted as part of Zambia's request.

Annex 2.4: Recommendations for conditional approval, by country

(in alphabetical order)

1. BOSNIA & HERZEGOVINA *(New application)*

New and under-used vaccines sub-account, hepB: Conditional approval

Conditions required:

- Provide the ICC work plan for the next 12 months, including activities to strengthen the ICC.
- Progress report on the implementation of recommendations from the immunization assessment.
- Provide a more operational introduction plan for hepB vaccine.
- Complete tables on five-year budget, and provide strategic directions towards financial sustainability.
- Reconcile figures between tables.

2. NIGERIA *(New application)*

New and under-used vaccines sub-account, yellow fever: Conditional approval

Conditions required:

- Provide an introduction plan for yellow fever vaccine, in accordance with GAVI guidelines on the introduction of new and under-used vaccines.

Hepatitis B vaccine: Nigeria is not eligible since its DTP3 coverage is less than 50%.

3. ZIMBABWE *(Re-submission)*

New and under-used vaccines sub-account, DTP-hepB-Hib: Conditional approval

Conditions required:

- Detailed introductory plan for DTP-hepB-Hib vaccine, taking into account the experience of two-year introduction of hepB (in combination with DTP) into Zimbabwe's routine immunization programme.
- Confirmation that GAVI funding will not replace government funding for the current DTP-hepB vaccines, and how funds thereby saved will be used for immunization purposes.

Annex 2.5
Recommendations for re-submission, by country

(in alphabetical order)

1. DJIBOUTI *(New application)*

Immunization services sub-account: Re-submission

The Review Committee recommends that Djibouti addresses the following points in its re-submission:

- Provide a more comprehensive immunization review (including injection safety and surveillance) and incorporate findings to update the multi-year plan, involving ICC and partners in the country.
- Provide a work plan for ICC for the next 12 months.
- Produce a more achievable target of immunization coverage and reduction of vaccine wastage rate.
- Provide a progress report on the implementation of recommendations from the immunization reviews.
- Clarify sources of EPI financing.

2. ERITREA *(New application)*

Immunization services sub-account: Re-submission

Eritrea will only be eligible if it can provide reliable data that DTP3 is less than 80% by 12 months of age.

The Review Committee recommends that Eritrea address the following points in its re-submission:

- Provide clear indications on target number of children to be immunized.
- Provide target for immunization coverage and vaccine wastage rate.
- Provide a strategic direction for resource mobilization.

3. SUDAN *(Re-submission)*

Immunization services sub-account:	Re-submission

The Review Committee recommends that Sudan address the following points in its re-submission:

- Broaden participation by ICC in the development of applications and resource mobilization.
- Justify which figures will be used: coverage survey or administrative reports for re-calculation of number of children targeted for immunization.
- Ensure the multi-year plan integrates and implements recommendations from the immunization assessments, including plans for injection safety, and reduction of wastage and drop-out rates.

4. TOGO *(New application)*

Immunization services sub-account:	Re-submission
New and under-used vaccines sub-account, DTP-hepB-Hib & yellow fever:	Re-submission

The Review Committee recommends that, in its re-submission, Togo should:

- Revise the multi-year plan, incorporating results of its EPI review, and provide an introduction plan for hepB, Hib and yellow fever vaccines, including cold-chain capacity requirements, safety injection plans, training of health workers, and social mobilization (refer to GAVI guidelines).

5. YEMEN *(Re-submission)*

New and under-used vaccines sub-account, DTP-hepB-Hib:	Re-submission

Before re-submitting, the Review Committee recommends that Yemen clarify its immunization coverage to be eligible (DTP3 over 50%) for the new vaccine. If eligible, Yemen is urged to:

- Provide a detailed introduction plan for new vaccines in accordance with GAVI guidelines on the introduction of new and under-used vaccines.
- Revise the multi-year plan and integrate recommendations from recent immunization assessments.
- Provide strategic directions towards financial sustainability.
- Provide a comprehensive plan on injection safety and sharps management.

Annex 2.6
Members of the Independent Review Committee

4th Round, May 2001

Dr Sam Adjei, Deputy Director-General, Ghana Health Services, Ghana

Dr Caroline Akim, Project Manager, Expanded Programme on Immunization, Ministry of Health, Tanzania

Dr Abdallah Bchir[1], Professor, School of Medicine, Monastir, Tunisia

*Mr Oleg Benesh[2], Epidemiologist, National Centre of Preventive Medicine, Moldova

Dr Merceline Dahl-Regis, Chief Medical Officer, Ministry of Health, Bahamas

*Dr Basile Kollo, Director of Community Medicine, Ministry of Health, Cameroon

Mr Robert Steinglass[3], Immunization Team Manager, BASICS, USA

Dr Viroj Tangcharoensathien (Chairperson), Health Systems Research Institute, Thailand

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* New members of the Review Committee.

1 Dr Bchir did not participate in the decisions on Afghanistan, Sudan, and Yemen.

2 Mr Banesh did not participate in the decisions on Bosnia & Herzegovina, and Turkmenistan.

3 Mr Steinglass did not participate in the decision on Nigeria.

Annex 3
Improving the safety of immunization programmes

Annex 3.1
GAVI and The Vaccine Fund support
GAVI policy statement

Each year, the over-use of syringes and unsafe injection practices worldwide combine to cause an estimated 22.5 million hepatitis B virus infections, 2.7 million hepatitis C virus infections and 98,000 HIV infections. Injections given as a part of immunization programmes account for a very limited proportion – approximately 5% of the injections delivered – and are widely considered the safest injections delivered. There is, however, a growing body of data demonstrating that the safety of immunization programmes throughout the world needs to be improved. Among unsafe practices, the re-use of syringes and/or needles without sterilization is of particular concern.

Based on the principle of "do no harm" we, the GAVI partners, acknowledge the importance of improving the safety of immunization programmes and have focused special attention on safety in relation to the other elements of immunization programmes.

- We commit to *The WHO/UNICEF/UNFPA/IFRC joint statement on the use of auto-disable syringes in immunization services*[1] which calls for the exclusive use of auto-disable (AD) syringes for all immunizations by the end of 2003; and we request WHO to finalize a statement, for our approval, on medical waste disposal – focusing particularly on waste in immunization programmes.

- In recognizing the above joint statement, we acknowledge our roles and responsibilities with regard to improving the safety of immunization programmes. For instance, national partners that support the purchase of vaccines will also finance an appropriate number of AD syringes and provide for the safe management of wastes for those vaccines.

- We also commit to use the *Aide-Mémoires* on injection safety[2] and on health-care waste[3] to guide investments and efforts to improve the safety of injections in immunization programmes, and thus serve as a model for other sectors of health programmes.

1 *Safety of injections*, Department of Vaccines and Biologicals,World Health Organization, Geneva. WHO&V&B/99.25, December 1999. Attached as Annex 3.2.

2 *Aide-Memoire for a national strategy for the safe and appropriate use of injections*, (Secretariat of the Safe Injection Global Network, World Health Organization, Geneva). Attached as Annex 3.3.

3 *Aide-Memoire for a national strategy for health-care waste management* (Department of Protection of the Human Environment, World Health Organization, Geneva. September 2000). Attached as Annex 3.4.

- To assist countries in their efforts to improve the safety of immunization programmes and to transition to full use of AD syringes, we request that the Vaccine Fund, in addition to supplying AD syringes and safety boxes for Vaccine Fund-supplied vaccines, also provide ADs for all traditional routine EPI vaccines or the equivalent amount of money – for three years, to all countries that received approval for applications submitted for either of the Vaccine Fund sub-accounts. The AD syringes (or their equivalent in funds) will provide countries and their partners with the opportunity to begin improving the safety of their programmes immediately, while they are identifying other sources of funds to support a national plan to improve safety and medical waste disposal.

  Funds will be awarded based on a review of the injection safety plan component of the country application to GAVI. These plans must describe a process for developing national policies and plans of action, and document national/partners' commitment to improve the safety of the immunization programme. Countries that have already received awards will be asked to ensure that their injection safety plan is complete, as described in the revised application guidelines, and submit it to the GAVI Secretariat. (India, Indonesia and China will also be eligible, but as these negotiations are be done on a country-by-country basis, they will be handled individually.)

- Recognizing that safety will not be improved solely by the provision of technology, we also commit to a long-term communication effort to increase awareness of the severity of the problem of unsafe injection practices and to advocate for behavior change, both among health providers and recipients. This effort will be led by WHO, UNICEF and the GAVI Advocacy Task Force.

- As a centre-piece of these efforts, GAVI partners will monitor improvement in the safety of national immunization programmes in a fashion that will encourage national governments and their partners to give similar attention to safety as that given to expanding DTP3 coverage. In the context of monitoring progress, safety will be recognized as a sentinel of overall programme quality. We request the Task Force for Country Coordination to develop means for monitoring safety and to highlight safety with special emphasis while developing guidelines for the preparation of annual reports and mid-term reviews.

- Finally, we acknowledge that appropriate disposal of medical waste is an important element in efforts to improve the safety of national immunization programmes and should be based on the principle that the "polluter pays". Although we realize that there are very limited environmentally sound options for safe waste elimination, we commit to supporting countries in their immediate action, using the best practices available to minimize the risk of exposure to medical wastes for staff and the community. We encourage fellow GAVI partners to invest in the development of environmentally sound, reasonably priced methods for disposing of medical wastes.

Annex 3.2

Safety of injections

WHO-UNICEF-UNFPA joint statement* on the use of auto-disable syringes in immunization services

1. The reuse of standard single-use disposable syringes[1] and needles places the general public at high risk of disease and death.
2. The auto-disable syringe, which is now widely available at low cost, presents the lowest risk of person-to-person transmission of blood-borne pathogens (such as Hepatitis B or HIV) because it cannot be reused. The auto-disable syringe is the equipment of choice for administering vaccines, both in routine immunization and mass campaigns.
3. "Safety boxes", puncture-proof containers - for the collection and disposal of used disposable and auto-disable syringes, needles and other injection materials - reduce the risk posed to health staff and the general public by contaminated needles and syringes.
4.
   - WHO, UNICEF and UNFPA reaffirm the current policy that auto-disable syringes, vaccines and safety boxes should continue to be supplied as a "bundle" *(see box, page 4)* for all elective and emergency campaigns.
   - UNICEF reaffirms its current policy that UNICEF programme funds cannot be used to procure standard disposable syringes for any immunization purpose.
   - UNICEF announces that, as of 1 January 2001, no procurement service contracts[2] for standard disposable syringes will be entered into.
   - WHO, UNICEF and UNFPA urge that, by the end of 2001, all countries should use only auto-disable syringes or syringes which are designed to be sterilized. Standard disposable syringes should no longer be used for immunization.
   - WHO, UNICEF and UNFPA urge that, by the end of 2003, all countries should use only auto-disable syringes for immunization.
5. All partners of immunization services are requested to finance not only the vaccines, but also the safe administration of vaccines, auto-disable syringes and safe management of waste. Partners should do this by planning and implementing the above strategy, as well as by supporting related training, supervision and sensitisation activities.

***This joint policy statement revises and replaces the document *WHO-UNICEF policy statement for mass immunization campaigns*, WHO/EPI/LHIS/97.04 Rev.1. It is issued by the World Health Organization, Geneva, Switzerland (Department of Vaccines and Biologicals), the United Nations Children's Fund (UNICEF Programme Division, New York, USA and UNICEF Supply Division, Copenhagen, Denmark) and the United Nations Population Fund, New York. This policy is also the adopted practice of the International Federation of Red Cross and Red Crescent Societies in their operations.**

Background

Information reaching WHO, UNICEF and UNFPA consistently highlights the widespread occurrence of unsterile injection practices and identifies a major cause as insufficient supplies of syringes and needles[3]. Unsafe injections can result in the transmission of blood-borne pathogens from patient-to-patient, patient-to-health worker and, more rarely, health worker-to-patient. The community at large is also at risk when injection equipment is used and then not safely disposed of. In many instances, used equipment is reused, sold or recycled because of its commercial value. The imperative to improve safety of injections in immunization services is underlined by the publication of articles in the *WHO Bulletin* (October 1999) which show that, although immunization injections are thought to be safer than curative injections, around 30% of immunization injections are still unsafe. Much evidence of reuse of disposable syringes exists and even recent country reviews suggest that sterilization of syringes and maintenance of sterilization equipment is not systematic.

Last year, in the developing world, routine immunization of children under one year and immunization of women of childbearing age with tetanus toxoid (TT) accounted for over one billion injections. In addition to routine immunizations, measles control/elimination activities and disease-outbreak control operations together delivered more than 200 million injections in the same year.

Hepatitis vaccine is now in use in half of the developing countries and Hib, measles-mumps-rubella (MMR) and pentavalent vaccines are already widely used in the Americas. Acceleration of special activities which aim at the elimination of maternal and neonatal tetanus and at better control of measles has begun. And a Global Alliance of Partners of Immunization Services (GAVI) is being formed to assure access to new vaccines for many of the poorest countries where the vaccines are needed most.

These increases of immunization services, including the elimination and control campaigns, offer an opportunity for improvement and make it imperative that injections are made safe for people.

The disease burden associated with unsafe injection practices has been estimated[4] and the cost implications of treatment of these diseases has been quantified[5]. Each unsafe injection costs governments between three to five times the extra cost of auto-disable syringes (which guarantee a sterile injection), not to mention the toll in terms of human suffering.

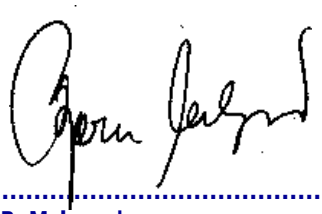
Strategy

Over the past years, WHO, UNICEF and UNFPA have launched a number of initiatives which aim to improve the safety of injections. The most recent was the precursor to this joint statement in 1997[6] which related to the use of auto-disable syringes and safety boxes in immunization campaigns. That policy has assured the simultaneous budgeting and parallel purchasing and shipping of sufficient syringes and safety boxes for each consignment of vaccines for mass campaigns. Now, with a broad experience of the use of this equipment in the field, is the time to consolidate a policy to cover all administration of vaccine.

WHO and UNICEF have agreed to implement a strategy to ensure that special attention is paid to the safe administration of vaccines, both in routine immunization services and during mass campaigns. The policy statement *(on page 1)* defines the position of WHO and UNICEF and is intended as a guide to other partners of immunization services, including national ministries of health.

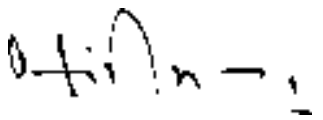
In addition to this policy statement, WHO and UNICEF recommend that:

- Countries exert maximum effort to ensure that procedures for injection safety are rigorous -this includes routine use and monitoring of indicators of sterilization while sterilizable equipment is still used. Partner agencies involved in immunization programmes in countries should provide maximum support for the strengthening of safe injection practices.
- Urgent attention be given to develop appropriate tools (current monitoring tools are still insufficient to objectively demonstrate compliance to safe injection practices).
- Agencies supporting immunization services be encouraged to provide time-limited financial support to countries procuring standard disposable syringes for immunization until government-won budgets can be increased to cover the additional cost of auto-disable syringes.
- Agencies supporting immunization services which fund the purchase of locally-manufactured standard disposable syringes for immunization should assist countries with technology transfer to enable them to switch to auto-disable syringes in the shortest possible time.
- Used auto-disable syringes should be deposited in safety boxes without re-capping, burned locally and the remains buried underground - until improved disposal methods are developed. Urgent attention should be given to develop improved means for effective, safe and environmentally-acceptable waste processing and final disposal of auto-disable syringes.



B. Melgaard
Director, Vaccines & Biologicals
World Health Organization

V. Li-Frankenstein
Director, UNICEF Supply Division
United Nations Children's Fund,
Copenhagen



S. Rasheed
Director, UNICEF Programme Division
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New York

M. Nizamuddin
Director, Technical and Policy Division
United Nations Population Fund

Ibrahim Osman
Under Secretary General, National Society,
Cooperation and Development (NSCD),
International Federation of Red Cross
& Red Crescent Societies

FOOTNOTES

[1] Auto-disable (A-D) syringes conform to the WHO/V&B Performance Specifications E8/DS1 and DS2 and include pre-filled pouch-and-needle injection devices. This statement applies only to available supplies of A-D syringes.

[2] UNICEF procurement service contracts cover the procurement of supplies and equipment by UNICEF as a service to governments and other organizations.

[3] Review: Unsafe injections in the developing world and transmission of blood-borne pathogens, Simonsen L (Ph.D.), Kane A, Lloyd J, Zaffran M, Kane M (M.D.), *WHO Bulletin* October 1999.

[4] Unsafe injections in the developing world: Region based estimates of the transmission of blood-borne pathogens, Kane A et al. *WHO Bulletin* October 1999.

[5] Direct and indirect costs of alternative injection technologies used in immunization services, Ekwueme et al. (Unpublished study with WHO, October 1999.)

[6] Safety of Injections: WHO-UNICEF policy statement for mass immunization campaigns, WHO/EPI/LHIS/7.04 Rev.1 – replaced by this statement, WHO/V&B/99.25.

The term "bundling" has been chosen to define the concept of a theoretical "bundle" which must comprise each of the following items:

- Good quality vaccines
- Auto-disable syringes
- Safety boxes

The implication is that none of the component items can be considered alone; each component must be considered as part of a "bundle" which contains the other two. "Bundling" has no physical connotation and does not imply that items must be "packaged" together.

Copies and information may be requested from:

World Health Organization (WHO)
Department of Vaccines and Biologicals, 20 Avenue Appia, CH-1211 Geneva 27, Switzerland
Phone: +41 22 791 4373; Fax: +41 22 791 4193; E-mail: gpv@who.ch

United Nations Children's Fund (UNICEF)
3 United Nations Plaza, New York, NY 10017, United States of America
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United Nations Children's Fund (UNICEF)
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United Nations Population Fund (UNFPA)
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International Federation of Red Cross and Red Crescent Societies (IFRC)
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Ordering code: WHO/V&B/99.25. Printed: December 1999

Annex 3.3

WORLD HEALTH ORGANIZATION

Injection Safety

AIDE-MEMOIRE

for a national strategy for the safe and appropriate use of injections

A safe injection does not harm the recipient, does not expose the provider to any avoidable risks and does not result in any waste that is dangerous for other people.

Worldwide, each year, the overuse of injections and unsafe injection practices combine to cause an estimated 8 to 16 million hepatitis B virus infections, 2.3 to 4.7 million hepatitis C virus infections and 80,000 to 160,000 HIV infections*. Among unsafe practices, the re-use of syringes and/or needles without sterilization is of particular concern.

Injection-associated transmission of bloodborne pathogens can be prevented through the development of a strategy to reduce injection overuse and achieve injection safety and its implementation by a national coalition, with the assistance of a coordinator.

The three elements of a strategy for the safe and appropriate use of injections are described in detail overleaf:

- Behaviour change among patients and healthcare workers to decrease injection overuse and achieve injection safety
- The availability of necessary equipment and supplies
- The management of sharps waste.

Words of advice

- **Conduct an initial assessment**
- **Secure government commitment and support for the safe and appropriate use of injections**
- **Establish a national injection safety coalition, coordinated by the Ministry of Health**
- **Develop a national policy and plan**
- **Develop a systematic strategy for behaviour change among patients and healthcare workers to decrease injection overuse and achieve injection safety**
- **Ensure the continuous availability of injection equipment and infection control supplies**
- **Set up a waste management system for the safe disposal of sharps**
- **Monitor the impact of activities on injection frequency, injection safety and injection-associated infections**

* Kane A et al. *Bull World Health Organ* 1999; 77: 801-807.

Checklist

National policy on the safe and appropriate use of injections

- ❑ Assessment of injection practices
- ❑ Coordination of injection safety
- ❑ Multidisciplinary national coalition
- ❑ National policy and plan
- ❑ Costing, budgeting, and financing
- ❑ Three-point strategy for the prevention of unsafe injection practices
- ❑ Monitoring and evaluation

Behaviour change

- ❑ National behaviour change strategy
- ❑ National standards for injection safety
- ❑ Incorporation of safe injection practices into minimum standards of care
- ❑ Promotion of safe technologies
- ❑ Promotion of rational use of injections
- ❑ Other components of behaviour change

Equipment and supplies

- ❑ Auto-disable (AD) syringes for immunization
- ❑ Appropriate types of syringes and needles for curative care
- ❑ Norms and standards for equipment
- ❑ Central bulk procurement, including safety boxes
- ❑ Central management of storage
- ❑ Efficient distribution system

Management of sharps waste

- ❑ Policy for sharps waste
- ❑ Assessment of waste management system
- ❑ Selection of appropriate waste disposal systems
- ❑ Regulatory framework
- ❑ Adequate resources
- ❑ Implementation of waste management system
- ❑ Training and supervision

Key elements

National policy on the safe and appropriate use of injections

It is the responsibility of governments to ensure the safe and appropriate use of injections.

The achievement of this goal requires the establishment of a national multidisciplinary coalition involving different departments of the Ministry of Health and other stakeholders, such as non-governmental organizations and associations, and private healthcare providers.

The coalition should be coordinated by a Ministry of Health team and should receive political support, adequate funding and trained staff.

Important activities include:

- Initial assessment of injection frequency, breaks in injection safety and adverse events associated with injections, including a behavioural and systems analysis
- Establishment of an injection safety unit to coordinate departments of the Ministry of Health, including health promotion, immunization, family planing, essential drugs programmes, healthcare service delivery, nosocomial infections, blood transfusion service and waste management
- Establishment of a national coalition, including WHO, universities, non-governmental organizations, behaviour change specialists and associations (e.g. consumers, public and private healthcare workers, traditional practitioners)
- Development of a national policy and plan (including costing, budgeting, and financing) by the national coalition, within the Ministry of Health's overall plan of action
- Prevention through behaviour change to reduce injection overuse and achieve injection safety; provision of sufficient quantities of injection equipment and infection control supplies; and management of sharps waste
- Monitoring of the impact through process indicators (injection frequency and injection safety) and outcome indicators (incidence of injection-associated infections, rational use of injections)

Behaviour change

The foundation for the safe and appropriate use of injections is a behaviour change strategy targeting consumers as well as public, private and lay healthcare workers.

Important activities include:

- Development of a national communication and behaviour change strategy on the basis of behaviour and systems analysis
- Definition of national standards for safe injection practices
- Incorporation of injection safety into minimum standards of care
- Promotion of safe technologies
- Promotion of the rational use of injections within essential drug programmes (e.g. restriction of unnecessary injectable drugs) and with the private sector
- Addressing issues that may lead to poor injection practices, including attitudes, emotions, incentives, beliefs, power relationship, norms and systems

Equipment and supplies

Eradication of the re-use of syringes and needles without sterilization requires the continuous, sufficient availability of injection equipment and infection control supplies in all healthcare facilities.

Important activities include:

- Adoption of auto-disable (AD) syringes for immunization
- Selection of appropriate types of syringes and needles for curative care (sterilizable, disposable or auto-disable)
- Enforcement of international norms and standards by the national regulatory authority
- Central bulk procurement of injection equipment and infection control supplies, including safety boxes
- Central management of storage
- Efficient distribution system to ensure continuous, sufficient availability in all healthcare facilities nationally

Management of sharps waste

The efficient, safe and environmentally-friendly management of sharps waste is the only means of ensuring that disposable syringes and needles are not re-used and do not lead to accidental needlestick injuries.

Important activities include:

- Formulation of a policy stating that disposal is part of the syringe lifecycle and that healthcare services have a duty to manage sharps waste
- Assessment of the waste management system, including expressed and real needs
- Selection of appropriate waste disposal systems for all levels of healthcare facilities
- Implementation of a regulatory framework
- Identification of human and financial resources required
- Implementation of a waste management system
- Training and supervision

Additional information on the safe and appropriate use of injections can be obtained on the World-Wide Web at www.injectionsafety.org and on the Safe Injection Global Network internet forum at sign@who.int

Annex 3.4

WORLD HEALTH ORGANIZATION

Safe health-care waste management

AIDE-MEMOIRE

for a national strategy for health-care waste management

Health-care waste is a by-product of health care that includes sharps, non-sharps, blood, body parts, chemicals, pharmaceuticals, medical devices and radioactive materials. Poor management of health-care waste exposes health-care workers, waste handlers and the community to infections, toxic effects and injuries. It may also damage the environment. In addition, it creates opportunities for the collection of disposable medical equipment (particularly syringes), its re-sale and potential re-use without sterilisation, which causes an important burden of disease worldwide.

The most important principles underlying effective programmes for the management of health-care waste include, firstly, the assignment of legal and financial responsibility for safe management to the waste producer; and, secondly, the responsibility of duty of care. Precaution should be applied whenever risks are uncertain.

It is essential that everyone concerned by health-care waste should understand that health-care waste management is an integral part of health care, and that creating harm through inadequate waste management reduces the overall benefits of health care.

Policies and plans for the safe management of health-care waste should address the following three elements:

1 The establishment of a comprehensive system of health-care waste management, from the generation of waste to its disposal – to be implemented gradually.

2 The training of all those involved and increasing awareness.

3 The selection of safe and environment-friendly options for the management of health-care waste.

Words of advice

- **Secure government commitment and support for safe health-care waste management**
- **Conduct an initial assessment of the situation of potential harms from health-care waste**
- **Manage waste comprehensively, addressing responsibilities, resources, waste minimization, handling and disposal**
- **Raise awareness among those responsible for regulating, generating and handling waste and provide training in safe practices**
- **Select safe, environment-friendly and sustainable waste management options**
- **Monitor and evaluate waste management activities and their impact**

Checklist

for action at national and local level

National policy for safe health-care waste management

- ❑ Designation of responsible authority
- ❑ Regulatory framework and guidelines
- ❑ Initial assessment
- ❑ Integration into overall waste management plan
- ❑ Monitoring and evaluation

Comprehensive system of health-care waste management

- ❑ Assignment of waste management responsibilities to personnel
- ❑ Allocation of resources
- ❑ Minimization of waste
- ❑ Segregation of waste
- ❑ Safe collection, handling and storage
- ❑ Safe treatment and disposal

Awareness and training

- ❑ Inclusion of waste management in the curricula of health-care personnel
- ❑ National training package
- ❑ Train the trainers programme
- ❑ Education on health risks
- ❑ Education on safe practices

Selection of options for the management of health-care waste

- ❑ Review of available options
- ❑ Checks of safety and environment-friendliness
- ❑ Ensure workers' safety
- ❑ Evaluation of sustainability
- ❑ Assessment of acceptability
- ❑ Monitoring of safety and efficiency

September 2000

Key elements

National policy for safe health-care waste management

It is the responsibility of governments to create a framework for the safe management of health-care waste and to ensure that health-care facility managers take their share of responsibility to manage wastes safely.

This requires a national coordinating mechanism involving the Ministry of Health and other stakeholders. It is important that a designated authority coordinates these efforts and receives sufficient political support, funding and trained staff.

Important activities for a national strategy to achieve safe health-care waste management include:

- Identification of key partners, including but not necessarily limited to: Ministry of Health, Environment Agency, non-governmental organizations, waste producers and waste disposal companies or services
- Designation of the responsible authority for policy formulation, implementation and evaluation
- Initial assessment and analysis of problems leading to unsafe handling or disposal
- Development of a national policy framework stating that the management of waste is part of the health-care system, and that health-care services should be assigned legal and financial responsibility for safe waste management and should manage their waste with duty of care
- Development of a regulatory framework and national guidelines, based on a comprehensive approach, including training, occupational health and safety issues and sound choices of waste management options, according to local circumstances
- Development of an enforcement mechanism
- Setting of practical targets or objectives over a specified time period
- Establishment of a national and regional infrastructure for health-care waste disposal
- Support of regional and municipal authorities in implementation
- Integration of waste minimization into national purchasing policies
- Routine monitoring of impact through process indicators (number of health-care establishments with safe waste management systems) and outcome indicators (e.g. number of accidents involving health-care waste).

Comprehensive system

Facilities that generate health-care waste should set up a comprehensive waste management system based on the most appropriate means of achieving the safe, environment-friendly management of waste. The system should start with basic measures and then gradually be improved. First steps should include the segregation and safe handling, treatment and disposal of sharps.

Important activities include:

- Assignment of responsibilities for waste management
- Allocation of sufficient human and financial resources
- Waste minimization, including purchasing policies and stock management practices
- Segregation of waste into harmful and non-harmful categories
- Implementation of safe handling, storage, transportation, treatment and disposal options
- Monitoring of waste production and waste destination.

Awareness and training

Awareness of the risks related to health-care waste and training in safe practices is essential in obtaining both commitment and behaviour change by all involved in the management of health-care waste.

Important activities include:

- Advocacy targeting policy makers and health-care facility managers regarding the risks and responsibilities related to health-care waste
- Inclusion of health-care waste management into the training curricula of nurses, doctors and health-care managers
- Development of a national training package, adapted to various professional categories
- Development of a 'train-the-trainers' programme
- Education of health-care and waste workers and the community on the risks associated with health-care waste and safe management practices.

Selection of options

Waste management options should be efficient, safe and environment-friendly to protect people from voluntary and accidental exposure to waste when collecting, handling, storing, transporting, treating or disposing of waste.

Important activities include:

- Identification of available centralized waste management and disposal resources
- Choice of sustainable management and disposal options, according to:
  - Affordability
  - Environment-friendliness
  - Efficiency
  - Workers' safety
  - Prevention of the re-use of disposable medical equipment (e.g. syringes)
  - Social acceptability
- Identification of appropriate options for all levels of health-care facilities
- Monitoring and evaluation of safety and efficiency.

Related documents and additional information on health-care waste management can be obtained on the World-Wide Web at www.healthcarewaste.org

Annex 4
Capacity building

Annex 4.1
Overview

Executive summary

- At its November 2000 Board meeting, the GAVI Board requested a paper defining the strategy for GAVI to build capacity among countries implementing the programmes being supported by the Global Fund for Children's Vaccines.
- GAVI partners define capacity-building as enhancing the ability of national immunization systems to increase and maintain access to immunization services, to decrease the burden of vaccine-preventable diseases, and expand the use of safe and cost-effective vaccines.
- The starting point of capacity is the ability to identify and document problems on the ground and the power to address them – in context and at the most appropriate level.
- For GAVI partners, capacity-building is a cross-cutting issue that involves its task forces (financing, advocacy, R & D and country coordination), the regional working groups and ICC partners at country level.
- GAVI's strategy to build capacity has two prongs:

  i) to use a systematic five-step approach (benchmarking, assessment, planning, implementation, and monitoring) at the national level to address gaps in the immunization systems; and

  ii) to map and coordinate GAVI partner activities at the global and regional levels to better understand and address relevant unfilled gaps and support country-level activities.
- Implementation of this strategy at the national level will differ from previous efforts in that it will encompass the WHO-defined operational elements of immunization systems (service delivery, vaccine supply and quality, logistics, surveillance, advocacy and communication), and it will also target and focus capacity-building activities on the three underpinning health system functions (financing, management, and strengthening of institutional and human resources). The strategy will emphasize links between national governance and broader health sector development.
- The five-step approach will use and strengthen the mechanisms already endorsed by the GAVI partners – that is, ICCs, assessments, and multi-year immunization plans.

- To minimize the burden in countries, the capacity-strengthening strategy will, as far as possible, use information already collected as part of the GAVI process.
- The next step will be to benchmark "best practices" and to test an operational framework for assessment and strengthening of national capacity-building in 10 to 12 high- and low-performing countries from different regions. This will contribute to the strengthening of the capacity-building component in multi-year plans and focus partner support at country level.

Annex 4.2
Strategic framework for assessing and strengthening the capacity of national immunization services
Background paper

1. Executive summary

This document describes the strategy and framework envisioned by the Global Alliance for Vaccines and Immunization (GAVI) to strengthen national immunization programmes (NIPs) through a sustainable increase in quality, efficiency and effectiveness of vaccination services.

The paper begins with a working definition of capacity-building and a conceptual framework to address strengthening of immunization programmes within the context of strengthening health systems, based on the approach outlined in the *World Health Report*[1] on health systems published in 2000. The paper describes a five-step process to strengthen the health system functions that underlie immunization services. The process will reinforce the effective implementation of three GAVI tools:

- comprehensive assessment to identify process and performance weaknesses;
- development and implementation of an achievable multi-year plan; and
- the monitoring of immunization services by ICCs and national authorities.

To judge the global impact of the capacity-building strategy, five targets areas are proposed, with specific indicators (some still under development) for each of the health system functions to be addressed. Indicators selected for implementing this process will be compatible with those addressed by the Common Assessment Tool and other tools used by GAVI task forces and partners, rather than introducing new ones.

Finally, the paper outlines specific activities for the national, regional and global levels and defines the next steps to be taken by GAVI partners and task forces in applying the framework. As an initial step, a specific focus on 8-12 countries is proposed.

Appendix 2 maps the existing capacity-building interventions currently being implemented by GAVI partners; it outlines the approach and indicates gaps that should be addressed.

2. Background

GAVI's strong interest in capacity-building is one of the factors which separates GAVI from previous global programmes supporting immunization. The GAVI partners' strong support of capacity-building and programme-strengthening initiatives is reflected by the commitment of the GAVI Board and its task forces to prioritize the development and implementation of an appropriate framework and strategy. This paper is the work of a small inter-task force subgroup composed of members from the three GAVI task forces.

[1] *World Health Report 2000 – Health systems: Improving performance.* World Health Organization, Geneva, 2000.

3. Definition of capacity building

Capacity building (CB), in the context of this paper, means to *significantly enhance the ability of national immunization programmes (NIPs) to increase and maintain access to immunization services, decrease the burden of vaccine-preventable diseases,* and expand the use of safe and cost-effective vaccines. Special attention will be given to:

- safety and quality;
- consistency with national health-sector goals;
- identification of funding shortfalls; and
- progress towards self-reliance in identifying and generating resources.

The systematic management of knowledge to retain work experiences and disseminate expertise throughout the organization is also essential.

Three GAVI goals are relevant to this definition:

1) By 2005: 80% of developing countries will have routine immunization coverage of at least 80% in all districts.

2) By 2002: 80% of countries with adequate delivery systems will have introduced HepB vaccine and, by 2007, 100%.

3) By 2005: 50% of the poorest countries with a high burden of disease and adequate delivery systems will have introduced Hib vaccine.

It is recognized that the CB process must maintain and develop existing abilities as well as develop new ones, and that it must be based on a methodology that can assess the current situation, define the future goals, and plot a way to reach them. It is also recognized that any CB strategy must address three levels: the individual, the institutions, and the overall health system.

4. Conceptual framework

This model describes the essential components for strengthening routine immunization services at country level. A framework that countries, as well as regional and global partners, can use to make the model operational is proposed in the document. The framework ensures that support for strengthening immunization services is well planned and appropriate, that it is consistent with global "best practices" and is effectively implemented and monitored.

4.1 Health systems functions

The *World Health Report*[2] defines four health systems functions that are essential to any health system:

- Stewardship, defined here as Management;
- Creating resources (investment and training), defined here as Strengthening human and institutional resources;
- Financing; and
- Service provision, defined here as Operations.

[2] *World Health Report 2000 – Health systems: Improving performance.* World Health Organization, Geneva, 2000.

Three of these functions are necessary to support the five operational components and facilitate efficient delivery of services (see Figure 1 below). The functions occur typically within a broader health systems context and, as part of a dynamic system, have broad areas of overlap that vary considerably from country to country, and even between regions of a country. Appendix 1 lists areas for which indicators should be developed for each function.

4.1.1 Health systems function: financing

- Reliable, realistic, multi-year financing strategies from governments, and partners where appropriate, to achieve current and future programme objectives.
- Includes costing, budgeting, and planning activities, mobilization of financial resources and efficient use of those resources.

4.1.2. Health systems function: management (stewardship)

- Programme management: establishing policies and priorities, forecasting needs, strategic planning, and stakeholder coordination.
- Human resource management: supervision, leadership and team-building.
- Task analysis and work delegation.
- Budgeting and forecasting.
- Monitoring and evaluating collected programme performance data to identify causes of problems and find effective solutions.

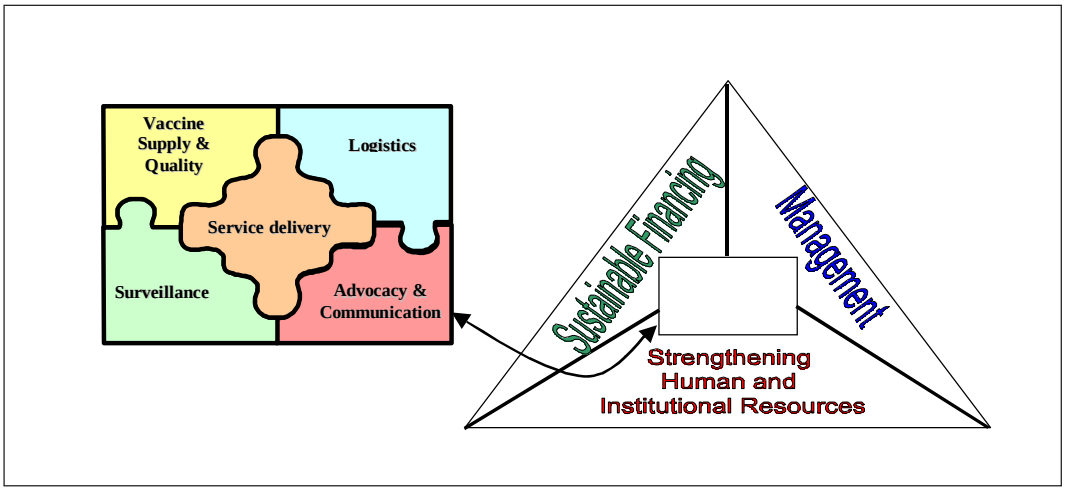
4.1.3. Health systems function: strengthening human and institutional resources (creating resources)

- Systematic and progressive strengthening of national institution/systems (e.g. strengthening national regulatory authorities, links to educational institutions and private sector expertise).
- Coordination of pre-service curricula with defined national health sector goals.
- Strengthening the abilities of health services personnel to identify and continually improve their knowledge, skills and expertise.
- Augmenting educational and research institutions to supply human and technical resources for long-term programme sustainability (e.g. increasing the importance of immunization services in the pre-service curricula of medical and nursing schools).
- Increasing the ability of regional partners to provide technical support for in-country activities.

4.1.4. Health systems function: operations (provision of services)

As depicted in Figure 1 below, the three health systems functions listed above provide the framework that supports the five operational components of a service-delivery programme. Together, these functions define any public-health delivery programme at country level – in this case, the delivery of immunization services.

Figure 1: Health system functions for immunization programmes



The operational areas of immunization services are seen as five interrelated and mutually dependent components.

- Service delivery: the strategies and activities involved in giving vaccinations (routine and supplemental activities).
- Vaccine supply and quality: forecasting vaccine needs; sourcing of quality vaccines; monitoring vaccine utilization.
- Logistics: delivery of vaccines and other equipment to the place of use, transport, cold chain and waste disposal.
- Surveillance: measurement of disease incidence, record keeping and reporting; laboratory testing.
- Advocacy and communication: immunization education and promotion; social mobilization; political and media advocacy.

4.2 Five-step approach for developing capacity

Based on universally-recognized management principles, a five-step approach has been defined for CB in countries.

- Benchmarking (process of defining "best practices"): This process defines the criteria and indicators for a well functioning service. Some would be specific global indicators useful for inter-country comparisons, while others would be nationally defined to help countries assess their progress over time.
- Assessment: Based on the indicators defined in the first step (*benchmarking*), the assessment is to identify gaps and document progress. GAVI partners have defined an overall assessment tool, the Common Assessment Tool, and a number of more specific assessment tools, such as the financing and injection-safety tools.
- Plan: In the GAVI context, there are a number of planning activities at country level, including multi-year strategic plans, annual work plans, and sub-national microplanning. These plans should address gaps identified in the assessments and so link directly back to the key indicators. Furthermore, plans should be

prioritized, they should indicate the activities needed to achieve milestones and the resources required; they should also identify responsible persons.

- Implementation: Implementation is putting the plan into operation. The aim here is to ensure that priority activities actually occur.
- Monitoring and evaluation: This is an essential step in the approach and sets the stage for a repetition of the cycle. A key monitoring element at country level will be the ICC or the national coordination mechanism.

This process builds on and strengthens the three key GAVI tools: the Common Assessment Tool, the multi-year plan, and the monitoring at national level by the ICC.

4.3. Global targets

The sub-group proposes that the following five target areas be defined at global level to help guide progress in strengthening immunization services:

1) Consistently high coverage over time in all districts, based on accurate population demographics (as accurate as possible).

2) Reduction of burden of vaccine-preventable diseases, consistent with global and regional targets and measured through quality surveillance systems.

3) Implementation of safe injection and waste disposal strategies; i.e. single sterile needle and a single sterile syringe to be used for each injection, then properly disposed of.

4) Parents' satisfaction with local services and a high percentage of parents expressing the desire for their children to be immunized.

5) Financial sustainability (as defined by the Financing Task Force).

Countries should be asked to identify their own indicators to measure progress towards these targets. The purpose of the targets is to assess progress across all health system functions at global level towards attaining the GAVI goals defined above.

5. Application of the strategy

5.1 At country level

It is proposed that 8-12 target countries be selected (one to three per region), in consultation with the regional working groups, to pilot efforts to achieve the GAVI goals. The approach should be most useful if activities are targeted primarily on the two functions which have been most neglected in the past – namely, Management, and Human and Institutional Resources. The global targets would then be used to assess the impact across countries, using a common level of performance.

5.2 Application at regional level

GAVI partners can use the approach to:

1) Develop tools for building capacity in a systematic way at national level, using Appendix 2 to help identify resources that are not currently being provided to countries.

2) Identify and address regional-level needs and weaknesses that are consistent across countries.

3) Aid regional working groups and partners to increase their capacity to provide countries with technical assistance and other resources.

5.3 Application at global level

GAVI partners can use the strategic framework to:

- Assess the impact of GAVI strategies, using the global targets and indicators defined by the Common Assessment Tool and those proposed by the task forces and subgroups in the areas covered by Appendix 1.
- Coordinate ongoing national, regional and international capacity-building strategies of global partners.
- Identify and move of global resources to fill gaps in a coordinated and comprehensive fashion (e.g. using the matrices in Appendix 2 to guide the development of needed global and regional resources). This would include high-level technical, reference and training materials that countries or regions may not be able to produce for themselves.
- Select approaches that may be universally applicable in CB activities, e.g. lead-country project, inter-country networks.

6. Next steps

To implement the strategy, a number of steps involve GAVI partners and entities such as its task forces and regional working groups. The key steps are outlined below:

6.1. For the Inter-Task Force Subgroup on Capacity Building

- Complete the benchmarking process, with input from many countries and partners to supplement the indicators already included in the Common Assessment Tool.
- Define a process to agree on global targets.
- Ensure that reports, submitted to the GAVI secretariat, on progress with funds from the Global Fund, include a section on CB.
- Complete the matrices mapping partner initiatives already in place.

6.2. For the Task Force on Country Coordination

- Coordinate the use of assessments in the three neglected health-systems functions to develop annual work plans.
- Work with the regional working groups to develop strategies for monitoring progress in strengthening capacities in immunization services delivery.

- Address the requirements for immunization advisers to support the needs of ICCs in their monitoring and coordination activities: select priority countries, and assign staff to fill the gaps.

6.3. For the Financing Task Force

- Complete the benchmarking process for the development of financial sustainability plans.
- Estimate the total amount of investment needed at each level for the activities for all health systems functions included to strengthen capacity in delivering immunization services for a minimum of selected representative countries; this could serve as a guide for countries.

6.4. For the regional working groups

- Identify the countries (one to three per region) to be targeted to pilot the capacity-building strategy. It is proposed that countries be identified to coincide with the assignment of immunization advisers.
- Using global targets to monitor annual work plans and progress.
- Develop annual reports on the impact of the strategy on countries.

6.5. For GAVI partners

In work that has already started, ensure support of the CB strategies defined in this document.

- Ensure that the revision of the Mid-Level Management Modules addresses all four health systems functions; not only operations/service provision.
- Support in-country activities to implement this strategy.

Appendix 1 to Annex 4.2: Proposed indicators for health-system functions

Countries should be asked to identify their own indicators to measure progress in addressing each of the health system functions. The sub-group will, in addition, suggest indicators – consistent with the five global targets – for each function. These indicators are to aid countries and regional working groups in performing needs assessments, developing plans that address gaps, and monitoring implementation.

Financing

The Financing Task Force is developing indicators on sustainable financing, linked with the development of a Financial Sustainability Plan. These will be considered at the June 2001 meeting.

Management

Indicators proposed:

1) Timeliness and completeness of reports, reflecting institutional capacity to monitor its own performance.

2) Provision of adequate immunization supplies – as indicated by lack of stock-outs.

3) Number of days spent by national management team members in districts (proxy for assessing supervision of sub-national activities and district micro-planning).

Strengthening human and institutional resources

Indicators proposed:

1) At each level, percentage of total staff who have received training in the past two years, including the specifics of those training activities.

2) A national training plan developed, funded and implemented.

3) Adequacy of staffing (country to define specific levels) – as indicated by the rate of staff turnover at relevant levels.

Operations/service provision

The Common Assessment Tool contains key indicators in each of the five areas of service delivery for immunization.

Appendix 2 to Annex 4.2: Capacity building activities under development or underway

Step	Financing	Operations	Management	Institutional strengthening
Benchmarking	FTF meeting to develop.	Common Assessment Tool under revision; Mid-level training modules being revised; Lead country project being developed by TFCC; Vaccine management training indicators done; ATF "best practices" being surveyed.	Need further development; Vaccine management training indicators done; ATF best practices being surveyed; Could use district health management training from AFRO as model.	Needed.
Assessment	Financing assessment tool exists; Insufficient capacity to do assessments; Annecy meeting gave general information.	13 countries have used Common Assessment Tool; Mid-level modules will include; Underway for vaccine; Management training; Annecy meeting gave general information.	Underway for vaccine management training; Needed for other areas.	Needed.
Plan	Required of GFCV countries at mid-term review; FTF meeting to develop structure; Should be addressed in mid-level modules.	Being addressed in mid-level modules; Lead country project and vaccine management training will address; Information on annual, multi-year planning at Annecy.	Multi-year plans, annual plans, district micro-planning in AFRO EPI planning guide; District health management training includes some elements; ICC facilitators may support.	Should be addressed in mid-level modules; District health management training includes some elements; ICC facilitators may support.
Implementation	Should be addressed in mid-level modules; ICC facilitators should provide support; Annecy meeting gave general information.	Mid-level modules will address ICC facilitators can assist Advocacy resource kit will address.	Should be addressed in mid-level modules; ICC facilitators should provide support; Need comprehensive approach.	Should be addressed in mid-level modules; ICC facilitators may support; Extensive consideration and work needed.
Monitoring	Annual reports to GAVI may cover Need to strengthen ICC role to monitor.	DQA reinforces reporting system Mid-term review addresses; Annual reports address; ICC facilitators can assist.	DQA supports strengthening system management; Mid-term review will address; Annual reports will address.	Needed.

Annex 5
Countries in complex emergencies

Annex 5.1
Update and policy recommendations

Background

- For the purpose of this analysis, we have used the UN Consolidated Appeals' definition of countries in "complex emergencies" *as countries with armed conflicts affecting large civilian populations through direct violence, forced displacement and food scarcity, resulting in malnutrition, high morbidity and mortality*.
- Emergencies can be considered in three phases: active conflict, chronic conflict, and rehabilitation (or development). An acute conflict usually generates sufficient funding for immunization through international appeals. However, this is not sustained; in a chronic conflict or rehabilitation phase, appeals are much less successful, leaving large gaps in the funding needs for immunization.
- Of the 28 countries classified as those experiencing complex emergencies, 22 are eligible for support from the Global Fund for Children's Vaccines (see Appendix 1 to Annex 5.2). Of these, 12 have been approved/recommended for support or conditional approval, 3 are preparing proposals, and 2 have been asked to re-submit. The status of 5 countries is currently unknown. Thus, the proposal process appears to be working for a majority of countries classified as experiencing complex emergencies.

Policy recommendations

1) To ensure sustained funding, GAVI could use its advocacy channels to encourage international and national authorities to include longer-term support to immunization services in their resource mobilization efforts during the acute conflict phase.
2) In countries with well-functioning national governments and relatively high immunization coverage, there may be vulnerable populations within their borders that are not reached by the health system. GAVI could encourage partners to ensure that immunization services are reaching those at risk.
3) In countries where governments are weak or non-functional, GAVI could consider proposals submitted by an operational partner or partners (such as WHO and UNICEF), engaging the multiple partners most suited to reach all parts of the countries (e.g., UNHCR, *Medicins sans Frontières*) with those partners taking responsibility for implementation.
4) The Independent Review Committee will continue on a case by case basis to highlight the complexities and programme challenges faced by countries in complex emergencies and take these into account when assessing the quality and appropriateness of their proposals. Innovative approaches needed to fulfill programme needs will be encouraged.

Annex 5.2
Immunization during complex emergencies

1. Introduction

At its November 2000 meeting in Noordwijk, the GAVI Board requested WHO and UNICEF to develop a GAVI strategy for countries affected by complex emergencies.

Such a strategy has significant importance for GAVI. A large number of unimmunized children live amidst armed conflicts and/or in "collapsed states". WHO has estimated that active transmission of vaccine-preventable diseases in these areas accounts for over 65% of internationally significant outbreaks. The primary goal of public health practitioners in complex emergencies is to reduce avoidable loss of life, a goal that is reflected in GAVI's stated mission to fulfil the right of every child to be protected against vaccine-preventable diseases.

In its first two years of operations, despite the relevance to its mission, GAVI has not specifically explored its mechanisms or capacity for supporting countries affected by complex emergencies. This paper has been developed by two WHO departments – Vaccines and Biologicals ; and Emergency Health and Action – with input from UNICEF, New York to explain complex emergencies, the role and importance of immunization in this context, GAVI's comparative advantages in such settings and how these advantages might be exploited.

2. Complex emergencies

For the purposes of this discussion, the term "complex emergencies" is restricted to *armed conflicts affecting large civilian populations through direct violence, forced displacement and food scarcity, resulting in malnutrition, high morbidity and mortality*. While there is no internationally-agreed scheme for classifying and describing complex emergencies, Table 1 below provides a working classification of the phases that countries, or areas of countries, may go through in the course of a complex emergency.

These phases have substantial implications for both the vulnerability of existing immunization systems and their capacity to deliver minimum services. It must be noted that complex emergency situations are, by nature, extremely fluid; for instance, a particular area of a country may rapidly move from one phase to another and, at any one time, different areas of the same country may be in different phases of emergency.

The magnitude of the problem posed by complex emergencies is reflected in Appendix 1 which lists all of the complex emergency-affected countries for which a UN Consolidated Appeal Process (CAP) was launched in 2001. According to the UN CAP over 40 million people, or 5-6 million children less than 5 years of age, are currently affected by complex emergencies in 15 countries.

Table I: Working scheme for the phases of a complex emergency

Parameters	Active conflict	Chronic conflict	Rehabilitation (or development)
Access and staff security	None, or extremely limited; no information on safety.	Uncertain, shifting access, but clearer information on security.	Improved access, but often haphazard insecurity.
Infrastructure, support and supply system	Ongoing attacks on key installations with disruption of basic services (e.g. electricity).	Assessments made; an ongoing degree of rehabilitation.	Rehabilitation of basic services, though often limited to main centres.
Main health services providers	International agencies, NGOs.	National health workers, often under contract with international agencies.	National health workers either under national authorities or contracted to international agencies.
Donors' focus	Emergency relief.	Emergency relief and rehabilitation.	Emergency relief and rehabilitation.
Focus of government and conflicting parties	Military aspects; conflicting parties unknown or not "officially" recognized.	Political and humanitarian aspects of the crisis.	Political value of humanitarian interventions.
Coordination of health activities	Precarious, often NGO or UN- led (Special Envoy and/or Humanitarian Coordinator).	UN mechanisms with international and local partner agencies (Red Cross, NGOs, etc.).	National mechanisms re-established with UN/NGOs in supporting roles.

Again, Table 1 is only a scheme to help understand the cycle of events a country, or part of a country, may be passing through when affected by a complex emergency. For example, in the Democratic Republic of the Congo the situation is extremely heterogeneous: the eastern region (Kivu, Kisangani) is in an acute crisis phase with little or no access to the affected population, the central region of Katanga is in a state of chronic conflict (in fact, the crisis is progressively diminishing), and the capital region of Kinshasa is in a rehabilitation (almost "normal") phase.

3. Immunization in complex emergencies

Vulnerability of services: Existing immunization services are particularly vulnerable to complex emergencies for a number of reasons. For example, routine service-delivery is usually heavily dependent on a functioning transport, communications and cold chain infrastructure. For strategic purposes, this infrastructure is among the things targeted during a conflict; this compromises the transport and storage of vaccines and immunization services, and leads to isolation of staff and irregular, if any, salary payments. In the absence of government structures (or unstable structures) there is little, if any, political commitment to vaccination delivery and surveillance. On the demand side the lack of peace and security rapidly shift the community demand from preventive services to exclusively urgent curative services.

Immunization service delivery in the setting of complex emergencies: The arguments for making immunization services the cornerstone of basic service-delivery in a complex emergency are compelling. First and foremost, vaccine-preventable diseases constitute the leading cause of preventable morbidity and mortality in such settings. Complex emergencies

result not only in a high incidence of vaccine-preventable diseases, but also in a marked increase in mortality. Measles is particularly notorious for spreading during emergencies to cause epidemics with case-fatality rates exceeding 35%. Despite the vulnerability of routine immunization services during complex emergencies, there is extremely good evidence that, with the appropriate strategy and resources, most vaccine-preventable diseases can be rapidly controlled through almost all phases of an emergency. However, complex emergencies are not homogeneous phenomena and there is no single solution – flexibility is the key.

The strategies for delivering immunization services in the setting of a complex emergency may differ considerably from a routine immunization programme in a stable setting. Table 2 highlights some of these differences.

Table 2: Comparison of immunization service-delivery strategies during complex emergencies and activities during routine immunization programmes

	Complex emergency	Stable situation
Strategy	Predominantly campaign-based (e.g. pulse immunizations, national immunization days [NIDs]).	Predominantly fixed sites with outreach and/or campaigns
Immunization calender (also see antigens below)	Per emergency guidelines (e.g., the age for measles immunization being reduced to six months).	Per national policy and law.
Target population	Denominator usually unknown. Age group extended to five years or more.	Based on census data. Children aged under one year.
Coordination and partnership		
• **Representatives of populations**	Faction leaders.	Minister of health.
• **Implementing agencies**	UN agencies, NGOs, religious organizations, volunteers, health-care providers from ministry of health.	Ministry of health and national government agencies.
• **Donor agencies**	Disaster/relief oriented (e.g. working group of the UN Inter-Agency Standing Committee).	Development oriented.
Disease surveillance	Rapid health assessment and detection of epidemics; international public health experts.	National public health institute.
Cold chain/logistics	"Fast chain" strategy; UN interagency humanitarian logistics, NGOs, militaries.	National infrastructure.

As noted above, there is considerable experience in delivering immunization in the context of complex emergencies. Examples include measles immunization in refugee camps, meningitis vaccination in sub-Saharan Africa, polio national immunization days (NIDs) worldwide and yellow fever campaigns in West Africa. On several occasions these activities, particularly NIDs, have contributed to a cessation of hostilities that could be exploited for broader purposes.

In addition to the marked differences in the strategies for delivering immunization in the setting of complex emergencies, there is usually a substantial difference also in the antigens that are delivered. This is for epidemiological and operational reasons. Table 3 below shows that the focus of immunization services in complex emergency settings is the rapid control of those diseases responsible for the highest morbidity/mortality and with the greatest epidemic potential. Other diseases of high mortality potential that are readily transmitted in setting with sub-optimal sanitation and hygiene are also priorities (e.g. tetanus).

Table 3: Traditional antigens targeted for use in each "phase" of a complex emergency

Antigens or intervention, in order of priority	Active conflict	Chronic conflict	Rehabilitation
Measles	+++	++	+
Poliomyelitis	+++	++	+
Vitamin A	+++	++	+
Yellow fever		++	+
Neisseria meningitides group A		++	+
DTP			+

Immunization activities in complex emergencies have helped foster links between health and other service providers. For example, linking measles vaccine delivery and food aid programmes in some complex emergencies has had a very positive impact, not only by saving children's lives but by also demonstrating the importance, value and feasibility of inter-sectoral interaction.

Other considerations: In addition to adapting service-delivery strategies to the realities of complex emergencies, successful immunization activities in these settings have also required:

- new partnerships, particularly to find solutions for logistics support (e.g., vaccine distribution within the context of UN interagency humanitarian logistics systems);
- a systematic dialogue with local nongovernmental authorities to negotiate access to populations affected by active conflict;
- negotiation with oversight authorities to ensure that interventions are consistent with the humanitarian principles of a health and human rights approach, opening humanitarian spaces and "doing no harm" (e.g. helping to shift power to nonviolent parties).

Appendix 1 to Annex 5.2: Countries and regions affected

	Countries and regions in complex emergency according to UN CAP 2001	Total population (*World Health Report 2000*)	Vulnerable population according to UN CAP	Eligible for Vaccine Fund?	Status of application to The Vaccine Fund [1]
1.	Afghanistan	21,923,000	10,400,000	yes	Approval recommended
2.	Albania	3,113,000	54,000	yes	Approval recommended
3.	Angola	12,479,000	1,900,000	yes	*Unknown*
4.	Bosnia & Herzegovina	3,839,000	1,163,000	yes	Conditional approval (recommended)
5.	Burundi	6,565,000	1,462,000	yes	In preparation
6.	Columbia	41,564,000	n/a	no	Not applicable
7.	Congo	2,864,000	644,000	yes	*Unknown*
8.	Côte d'Ivoire	14,526,000	202,000	yes	Approved
9.	Croatia	4,477,000	100,000	no	Not applicable
10.	DPR Korea	23,702,000	8,000,000	yes	*Unknown*
11.	Democratic Republic of Congo	50,335,000	2,487,000	yes	*Unknown*
12.	Eritrea	3,719,000	1,761,854	yes	Approval recommended
13.	Ethiopia	61,095,000	6,800,000	yes	In preparation
14.	Guinea	7,360,000	705,000	yes	Re-submission
15.	Liberia	2,930,000	1,500,000	yes	Approved
16.	Indonesia (Maluku Crisis & Timor)	209,255,000	500,000	yes	In preparation
17.	Iraq	22,450,000	n/a	no	Not applicable
18.	Kenya	29,549,000	4,000,000	yes	Approved
19.	Russian Federation (Chechnya)	147,196,000	330,000	no	Not applicable
20.	Rwanda	7,235,000	130,000	yes	Approved
21.	Sierra Leone	4,717,000	2,000,000	yes	Approved
22.	Somalia	9,672,000	4,000,000	yes	*Unknown*
23.	Sudan	28,883,000	4,000,000	yes	Re-submission (recommended)
24.	Tajikistan	6,104,000	1,200,000	yes	Approval recommended
25.	Macedonia	2,011,000	300,000	no	Not applicable
26.	Uganda	21,143,000	1,200,000	yes	Approved
27.	United Republic of Tanzania	32,793,000	484,000	yes	Approved
28.	Yugoslavia	10,637,000	722,800	no	Not applicable
	TOTAL	**496,780,000**	**40,168,854**		

[1] In summary, the status of applications submitted to The Vaccine Fund by the 22 eligible countries is: 12 approved/ recommended for approval or conditional approval; 2 re-submissions; 3 in preparation; and 5 unknown.

Annex 6
Working Group report on the alignment of GAVI objectives, ADC initiatives and other interventions

Annex 6.1
Overview

Executive summary

At its November 2000 meeting in Noordwijk, the Board requested the Working Group to consult with partners and prepare a paper:

> Outlining the strategies for integrating GAVI objectives with Polio Eradication and Measles Mortality Reduction Initiatives, including the:
>
> - transitioning of human resources, surveillance capacity and physical infrastructure;
> - adoption of joint milestones;
> - use of performance indicators;
> - integration of other interventions (e.g. Vitamin A).

The current immunization landscape is crowded with initiatives, goals and targets. With better alignment, the capacity to achieve all immunization goals will be greatly enhanced, including the GAVI routine immunization coverage target and the introduction of new vaccines. From a country perspective, improved alignment and coordination could benefit priority setting and efficiency of work[1]. Without better alignment there is a risk that the substantial investment and lessons of the Polio Eradication Initiative, in particular, will not be retained for the broader immunization agenda.

During the past six months, the Working Group has engaged in an intensive process of analysis and stakeholder consultation on alignment between GAVI and the accelerated disease control (ADC) initiatives i.e. polio, measles, maternal and neonatal tetanus (MNT), and vitamin A. To better align GAVI and ADC initiatives, the Working Group requests that the Board:

[1] Appendix 2 to Annex 6.2 shows the existing overlap between Vaccine Fund-eligible countries and ADC priorities.

Approve the immediate establishment a new ADC objective, milestone, and indicators as follows:

- New objective: To support the national and international accelerated disease control targets for vaccine-preventable diseases.
- New milestone: By 2005, the world will be certified polio-free.
- New indicators: Addition of disease outcome indicators. Selection of the most appropriate indicators (polio, measles, MNT and vitamin A) to be proposed by Working Group after consultation with partners.

Place renewed emphasis on GAVI's existing first objective "improve access to sustainable immunization services". This would serve to unify all immunization initiatives by making their primary aim to achieve "access to all children and target populations".

Successful integration with emphasis on "access" would require that, as soon as possible and no later than 2003, all countries' annual work plans, and subsequent multi-year plans, reflect an approach that incorporates routine services, accelerated disease control, introduction of new vaccines, and vitamin A supplementation within the context of the health system. Targets in the national plans would need to match available resources. For this approach to work, it would have to be technically and financially supported by all partners at all levels, especially through their participation in national and regional immunization coordinating committees (ICCs) and regional working groups.

The Working Group requests the Board to agree to consider, at an appropriate time in the near future, a revision of all GAVI objectives, milestones, and indicators to support the full operationalization of this strategic plan.

If the Board endorses this direction, over the next few months the Working Group would further elaborate the framework for this strategy and its implications for the national workplans and ICCs, and regional and global activities.

Immediately revise objective #2 as follows: "Expand the use of all existing safe and cost-effective vaccines, and promote delivery of other appropriate interventions at immunization contacts." [2]

Recognize the importance of a human resources infrastructure for immunization and request that UNICEF and WHO together develop, for consideration by the Board, an immunization human resources plan (i.e. minimum staff per country) and costing based on the current human resources, including those that are funded for ADC activities.

[2] Current GAVI objective #2 is to: Expand the use of all existing safe and cost-effective vaccines".

Annex 6.2
Integrating GAVI objectives with other health initiatives

1. Introduction

This report summarizes the extensive analysis and consultation process that has been carried out to develop a framework for GAVI to align its role in, and support of, all immunization initiatives. While this process has clearly demonstrated that there are compelling reasons for better alignment, it has also shown that true alignment could have significant implications for GAVI – not just in terms of its messages and activities, but also in enhancing its capacity to establish sustainable access to unreached children.

GAVI can play a catalytic role in re-integrating all aspects of immunization based on comprehensive multi-year planning at the country level, and sustainable technical and financial support for those plans through effective ICC mechanisms at national, regional, and global levels.

2. Context – achieving the best of both worlds

The starting premise for this discussion is that better alignment between GAVI and accelerated disease control (ADC) initiatives (i.e. polio, measles, MNT, yellow fever, and vitamin A) would be mutually beneficial and exploit synergies where they exist.

Accelerated disease control focuses on reducing childhood morbidity and mortality, fully exploiting the potential of existing vaccines by using intensive strategies to reach all children. To ensure success, these initiatives rely on strong surveillance and the use of disease impact indicators to drive activities. By its very nature, ADC is a time-limited, focused effort. A strategic link of all ADC initiatives is their reliance on strong routine immunization systems to sustain high coverage and the disease reduction impact achieved through mass campaigns. ADC initiatives have played a large role in maintaining the high visibility of immunization in both developing and donor countries.

In contrast, GAVI's approach is different. It focuses on a sector-wide approach to strengthen health systems, using funds from The Vaccine Fund, as well as unearmarked "shares", to supplement new vaccines. This allows countries to determine where funding should be directed to improve routine immunization coverage. The GAVI strategy is based on one comprehensive multi-year plan at country level supported technically and financially by an effective ICC mechanism. Performance is rewarded on the basis of increased DTP3 coverage achieved, rather than on reduction in childhood mortality or morbidity.

To many observers these differences have suggested that the immunization world is sometimes polarized between those who champion the urgency of using ADC to immediately reduce unnecessary childhood mortality, and those who argue that the primary effort must be to

strengthen routine immunization systems for potential long-term sustainability. The truth of the matter is that both approaches are important and can be mutually beneficial. However, continuation of the divide compromises the effectiveness of all immunization efforts.

Better alignment between the two approaches offers the opportunity to achieve an effective mix of health systems and targeted approaches. Through its strategies and innovations, ADC has redefined the notion of "routine immunization" by demonstrating that equitable access to all children is possible. Successful alignment would translate both the lessons and infrastructure of ADC to the broader immunization agenda – of particular relevance if GAVI's "routine immunization" target is to be achieved. Higher routine immunization coverage would in turn substantially facilitate the ADC targets. In the context of promoting health systems development and national priority setting, ADC efforts have been central to the development of multi-year immunization plans and ICCs.

3. Process and guiding principles

During the past six months, the Working Group (WG) has engaged in an intensive process of analysis and stakeholder consultation (Appendix 1) on alignment between GAVI and the ADC initiatives. At the request of the Working Group, WHO assigned a full time staff member and the Institute for Global Health assigned a half-time CDC-seconded staff member to assist with the analysis and manage the stakeholder consultation process.

Throughout, the Working Group has been mindful of the guiding principles to strengthen routine immunization, support country-determined priority setting, and build systems and human capacity to raise coverage. The topic of alignment was a priority agenda item at the last three Working Group meetings (Pretoria, Baltimore, Lyon). Work in progress was also presented and discussed in the weekly Working Group teleconference calls and in a special video conference in April.

The first methodological step was a "mapping" of the various immunization initiatives by their objectives, milestones, targets, partners, strategies, disease impact, available funding and funding gaps (Appendix 3). This analysis clearly demonstrated areas of existing overlap while pin-pointing differences. It confirmed that there is a strong foundation and clear justification for planning better synergies among initiatives.

Through the mapping exercise and subsequent stakeholder consultation, a framework of possible scenarios for alignment was developed for evaluation against four key areas of activity common to all initiatives:

- Advocacy: Behaviour change of donors, implementing partners, and countries.
- Fund-raising: Leveraging the resources to meet funding gaps.
- Coordination: Alignment of efforts/activities at global, regional, and country level.
- Country operations: Ensuring that the deployment of human and financial inputs is consistent with, and supportive of, national priorities.

4. Alignment framework and preferred scenario

Table 1 provides a summary of the alignment framework and the results of the stakeholder consultation on the preferred scenario (see Appendix 4 for more detailed analysis).

Table 1: Summary of the stakeholder consultation on GAVI/ADC alignment scenarios

Scenario	Implications			
	Advocacy	Fund-raising	Coordination	Country operations
1. Status quo	-	+	-	-
2. New objective milestone and indicators	+	+	-	-
3. New objective milestone/indicators and shared investment	+	+	+	+/-
4. Full integration of processes and funding	+	-	+	+

Key: + positive implications
- negative implications

Scenario 1 – the status quo: This was widely perceived as sub-optimal, and adversely affecting functions of advocacy and coordination, as well as country operations. Without attention to the childhood mortality impact of ADC, the credibility of GAVI can be challenged and its mission viewed as incomplete. Perhaps the only benefit to this scenario is that, maintaining independent fund-raising efforts, may lead to a net increase in international funding for childhood immunization.

Scenario 2 – in which GAVI adopts a new ADC objective and milestone, and incorporates ADC indicators: This received unanimous stakeholder support. Alignment at this level would benefit advocacy efforts and retain fund-raising autonomy. By adopting joint milestones (particularly for polio eradication) and indicators, GAVI would strengthen links to ADC, visibly affirm its support of globally declared targets for vaccine-preventable diseases (VPDs) and provide a call to action. On balance, however, the Working Group felt this scenario did not go far enough as it was unlikely to be sufficient to improve coordination at all levels or better facilitate country operations.

Scenario 3 – in which GAVI would make a shared investment in ADC, in addition to adopting a new objective/milestone, and selected ADC performance indicators: This would have greater positive impact overall. Benefits to advocacy efforts would be enhanced, while retaining the advantages of independent fund-raising. Importantly, strategic financial investment by GAVI in ADC would positively influence coordination and country operations (although countries would still have to deal with separate funding steams for respective initiatives).

Scenario 4 – the full integration of all financial support and processes (in addition to adopting a new objective/milestone and key indicators). It was agreed that, while this might optimize coordination and country operations, full alignment between GAVI and ADC initiatives is unrealistic and not operationally feasible at this time primarily because of differences in the stage of implementation, operating practices, and stakeholder profile of

the various initiatives. It is of particular concern that a single fund-raising mechanism might result in a slump in funding, a particular risk for polio eradication. In addition, some stakeholders indicated that they were not in favour of contributing to "one" fund for "all" immunization activities.

There was consensus among the Working Group and stakeholders that alignment scenario #3 – proposing that GAVI adopt a new objective/milestone, and selected ADC performance indicators, as well as a shared investment in ADC – was the preferred option to explore.

Section 5 outlines the options and implications of the preferred alignment scenario: polio, measles and MNT are dealt with below in Section 5.1 and "other interventions", such as vitamin A in particular, are subsequently addressed in Section 5.2.

5. Alignment of GAVI objectives and accelerated disease control: pros and cons

In seeking better alignment with ADC, the Working Group considered two strategic approaches:

i) Establish a new ADC objective, milestone and indicators.

ii) Place renewed emphasis on the existing GAVI "access" objective as encompassing ADC. At an appropriate time in the future (to be determined) propose a revision of all existing GAVI objectives, milestones and indicators to reflect innovative approaches to accessing all children and target populations, such as sustainable outreach systems, and the use of quality surveillance to monitor disease impact.

5.1 Polio, measles and maternal and neonatal tetanus (MNT)

The Working Group debated at length the pros and cons (Table 2 provides a summary) of the two strategies outlined above, as well as the time-frame. Some argued that it was not necessary, and was in fact damaging, for GAVI to have an explicit ADC objective. They felt that GAVI should move boldly to integrate ADC using its existing "access objective".

The Working Group agreed that the ultimate goal for alignment should place renewed emphasis on "access". However, the Working Group recognized that successful implementation of such a strategy would require time. Rather than choosing one approach over the other, it was proposed that, as an immediate step, GAVI would add an ADC objective, while having a clear vision in mind for expanding the existing "access" objective. A full review of all GAVI objectives, milestones and indicators would be required at a future point in time.

Establishing a new ADC objective, with emphasis on national decision-making, would serve to align GAVI with the ADC initiatives while firmly promoting the principle of responding to country-determined priorities. A new milestone would make explicit GAVI's commitment, already expressed in various documents, to the globally declared goals and targets for reducing vaccine-preventable child morbidity and mortality due to polio, measles and MNT, and strategically may bring new partners into the GAVI partnership (e.g. Rotary International). Adoption of selected new indicators would help leverage on-going country commitment to these important international disease control initiatives, which will be reaffirmed at the upcoming UN General Assembly Special Session on Children, September 2001.

Ultimately, there is potential for GAVI to lead a new vision for immunization by promoting the common platform of "access" already expressed in its existing first objective and which

is common to all immunization initiatives (ADC and routine). To truly operationalize this in a way that promotes alignment, revision of the milestone and addition of a "disease surveillance-based" indicator was considered by the Working Group as follows:

- Emphasize existing objective #1: Improve access to sustainable immunization services.
- Revise milestone: By 2005, 80% of children in all districts are accessed at least three times a year for immunization (ideally five contacts).
- Add ADC indicator: Measles mortality

The focus on accessing children with a minimum of at least three contacts per year would facilitate the achievement of all global immunization and mortality/morbidity reduction goals (polio, measles, MNT, yellow fever and vitamin A). It would allow the lessons of both ADC and routine approaches to combine when and where they are needed. The decision on the most appropriate strategy or methods to achieve the three contacts needs to be made at the country level. Enhancing the quality and management of fixed-site delivery of immunization services would continue to be the primary aim of GAVI to reach as many children as possible. However, recognizing that the GAVI goal of 80% DPT3 coverage can only be achieved through the use of multiple strategies, increased emphasis would be placed on revitalization of outreach and, if appropriate, periodic pulse/"catch-up" campaigns (e.g. multi-antigen "child health days").

A substantial implication of revising GAVI's first milestone is that it embraces greater equity by promoting 80% coverage in all districts. This change is proposed based on the evidence from the polio eradication initiative that 80% coverage is achievable in all districts when a comprehensive set of strategies is used.

While retaining the use of DTP3, the addition of a second indicator would be essential to promote the importance of high quality surveillance for monitoring the disease impact (morbidity/mortality) of immunization activities, a central precept of ADC. Potential indicators that were considered included “polio endemic status (yes/no)”; reduction in measles cases/deaths and/or number of MNT high-risk districts. Of these, measles mortality reduction is the preferred indicator.

Promotion of the cross-cutting issue of "access to children and target populations" would provide powerful opportunities for advocacy through use of the simplified key messages of "equity" and the use of immunization contacts to reduce, eliminate or eradicate morbidity due to vaccine-preventable disease. GAVI's identification with a less vertical, disease-specific approach would also exploit opportunities to add other interventions (such as vitamin A) with immunization contacts.

Profound conceptual change would be required for GAVI to reorient itself around an "access" platform. While this in and of itself would be a challenge, there is a risk that it may not be sufficiently explicit to convince ADC partners of GAVI's commitment to the global immunization targets. Moreover, irrespective of the exciting potential that change may offer, after only two-years of operations GAVI itself may be uncomfortable embarking on such a radical reorientation at this time. It may be preferable to think of this as a vision which GAVI wants to work towards over time in a more incremental manner.

After debating all the pros and cons of the two strategic directions (to establish a new ADC objective or place new emphasis on "access") the Working Group decided that it was not a question of "either/or" but rather a question of timing to do "both".

Table 2: Summary of pros and cons of strategic directions to facilitate better alignment with accelerated disease control (ADC) initiatives

Strategic direction	Pros	Cons
#1. Align by adding: **New objective:** To support the national accelerated disease control targets for vaccine-preventable diseases. **New milestone:** By 2005, the world will be certified polio-free. **New ADC indicators:** Selection of the most appropriate indicators (polio, measles, MNT, vitamin A) to be proposed by the Working Group in consultation with partners.	• Quick fix; GAVI reconciled with global immunization targets and initiatives. • Emphasis on national priorities consistent with GAVI's approach. • Visible statement about need to reduce VPD childhood morbidity/ mortality. • Balancing of "pushed by industry" image. • Performance indicators already being collected by GAVI partners (no additional work). • May bring in ADC partners to GAVI.	• Maintains a certain level of polarization between "routine" immunization and ADC by treating them separately. • GAVI's distinct focus on routine immunization and introduction of new vaccines is no longer as prominent.
#**2. Align by using existing objective #1** to promote common GAVI/ADC platform of "achieving access to children and target populations" and revise milestone, and add indicator: **Place renewed emphasis on existing objective #1:** Improve ***access*** to sustainable immunization services. **Revise milestone:** By 2005, 80% of children in all districts are accessed at least three times a year for immunization (ideally five contacts). **Add ADC Indicator:** • Measles mortality.	• Potential for GAVI to play leadership role and unify immunization initiatives by rallying around common issue of "access". • Embraces the strategies (campaigns, surveillance) and learning of ADC, increasing the chances of achieving GAVI's immunization coverage target. • Focus on minimum of three contacts a year would facilitate achievement of all global immunization and mortality/ morbidity reduction goals (polio, measles, MNT, yellow fever and vitamin A). • Measles indicator was originally proposed and included to monitor the first milestone. • Clear advantage for powerful advocacy message (equity and access). • Less vertical, non-disease specific approach, provides opportunity for adding other interventions (e.g. vitamin A).	• May be difficult to justify revising milestones within two years of GAVI's creation. • ADC partners may not be convinced. • GAVI's support of global immunization targets not explicit.

#1. Request to GAVI Board: Approve the immediate establishment a new ADC objective, milestone, and indicators as follows:

New Objective: To support the national and international accelerated disease control targets for vaccine-preventable diseases.

New Milestone: By 2005, the world will be certified polio-free.

New Indicators: Addition of disease outcome indicators. Selection of the most appropriate indicators (polio, measles, MNT and vitamin A) to be proposed by the Working Group after consultation with partners.

#2. Request to GAVI Board: Place renewed emphasis on GAVI's existing first objective "improve access to sustainable immunization services". This would serve to unify all immunization initiatives by making their primary aim achieving "access to all children and target populations".

Successful integration with emphasis on “access” would require that, as soon as possible and no later than 2003, all countries’ annual work plans, and subsequent multi-year plans, reflect an approach that incorporates routine services, accelerated disease control, introduction of new vaccines, and vitamin A supplementation within the context of the health system. Targets in the national plans would need to match available resources. For this approach to work, it would have to be technically and financially supported by all partners at all levels, especially through their participation in national and regional immunization coordinating committees (ICC's) and regional working groups.

At an appropriate time in the near future, agree to consider a revision of all GAVI objectives, milestones, and indicators to support the full operationalization of this strategic direction.

If the Board endorses this direction, over the next few months the Working Group would further elaborate on the framework for this strategy and its implications for the national workplans and ICCs, and regional and global activities.

5.2 Other interventions

The addition of an ADC objective and milestone proposed would serve to align GAVI and polio, measles and MNT, however, the issue of "other interventions" needs to be addressed separately.

There was stakeholder consensus that GAVI is missing an opportunity to promote the delivery of vitamin A at immunization contacts. Integration of vitamin A and immunization services has proven to be a tremendously successful marriage of two of the most cost-effective child health interventions available. By adding vitamin A to polio national immunization days (NIDs), it is estimated that over 400,000 child deaths were averted over the two-year period 1999-2000 alone. To ensure the ongoing provision of vitamin A to populations at risk of deficiency, it is important to promote administration with routine immunization services (both to post-partum mothers and children).

While GAVI should immediately promote vitamin A through immunization contacts, the stakeholder consultation found that in the near future other important interventions might also prove appropriate for delivery through immunization contacts. For example, preliminary research has shown the delivery of prophylactic malaria treatment with early immunization contacts to be a promising strategy for markedly reducing incidence in some areas. Thus,

GAVI should promote the inclusion of other interventions with immunization contacts if and when there is evidence to support them.

#3. Request to GAVI Board: Immediately revise objective #2 as follows: "Expand the use of all existing safe and cost-effective vaccines, and promote delivery of other appropriate interventions at immunization contacts."

6. Alignment: options and implications of shared investment

There was clear consensus throughout the stakeholder consultation that one of the greatest assets of the ADC initiatives was the infrastructure that had been established to pursue the specific ADC goals, particularly that of polio eradication. The importance of retaining this infrastructure and strategic approach for the benefit of all immunization initiatives was strongly voiced. The stakeholder consultation further found that of the major elements of the ADC investment, the human resources infrastructure was both the most important to GAVI goals and the most fragile in terms of financing beyond 2003 (indeed polio eradication staff capacity was already being scaled back in some regions). Investing in this human resource capacity would substantially facilitate GAVI's work in assessing immunization systems, preparing multi-year plans, ensuring interagency coordination (ICCs), and aligning activities at country, regional, and global levels.

As of 7 May 2001, 1555 staff were hired worldwide on polio-funding, with a mix of international (316) and national (1239) personnel representing a broad range of technical and support functions. These staff have been instrumental in building technical, managerial, and implementation capacity in countries and their terms of reference include the strengthening of routine immunization and surveillance activities. Retaining this resource would have substantial financial implications for the GAVI partners, with a recurring cost of between US$ 35-50 million per year at its current size.

#4. Request to GAVI Board: Recognize the importance of a human resources infrastructure for immunization and request that UNICEF and WHO together develop for consideration by the Board an immunization human resources plan (i.e. minimum staff by country) and costing based on the current human resources, including those that are ADC-funded.

Appendix 1 to Annex 6.2:
List of stakeholders consulted

1. American Red Cross (ARC)
2. BASICS
3. Bill & Melinda Gates Children's Vaccine Programme (CVP)
4. Centers for Disease Control (CDC)
5. Centers for Disease Control (CDC) Field Staff
6. GAVI Secretariat
7. Global Polio Technical Consultative Group (TCG)
8. Pan American Health Organization (PAHO)
9. Rockefeller Foundation
10. Rotary International
11. Task Force on Country Coordination (TFCC)
12. United Nations Children's Fund (UNICEF)
13. UNICEF Regional Immunization staff
14. United Nations Foundation (UNF)
15. USAID
16. World Health Organization (WHO)
17. WHO regional and country staff
18. World Bank
19. World Bank regional focal points

Appendix 2 to Annex 6.2: Overlap of Vaccine Fund-eligible countries and ADC priorities *(Draft dated 12.06.01)*

Vaccine Fund countries				Polio staff			Polio free	Measles (1997)	MNT (1998)	Yellow fever	Vitamin A
	Surviving Infants	DTP3 Coverage	Unimmunized population	International	National	Total	Risk	Deaths 0-4 years of age	Estimated deaths	Endemic countries	Status
India	22,646,467	78%	4,982,223	10	337	347	Priority	211,001	48,578		Clin.Def.
Nigeria	3,904,741	21%	3,084,745	39	118	157	Priority	131,807	34,583	Yes	Clin.Def
China	18,747,942	85%	2,812,191	4	1	5	Certified polio-free	2,343	8,627		Insuf.Dat/Lik
DR Congo	2,121,951	25%	1,591,463	14	134	148	Priority	53,744	10,019	Yes	Insuf.Dat/Lik
Indonesia	4,339,846	64%	1,562,345	1	6	7	Low risk	14,119	4,090		
Bangladesh	3,267,464	66%	1,110,938	12	48	60	Priority	20,152	10,386		Clin.Def
Pakistan*	5,014,610	80%	1,002,922	20	64	84	Priority	19,440	21,679		Clin.Def.
Afghanistan	986,568	9%	897,777	12	50	62	Priority	31,121	4,213		Sub-Clin.Def.
Ethiopia	2,444,650	64%	880,074	17	15	32	Priority	58,401	13,406	Yes	Clin.Def
Uganda*	996,151	51%	488,114	8	4	12	High risk	7,245	2,403	Yes	Clin.Def
Angola	534,375	22%	416,813	9	10	19	Priority	5,123	2,741	Yes	Clin.Def
Somalia	458,068	18%	375,616	9	19	28	Priority	19,981	8,791	Yes	Clin.Def
Niger	450,239	21%	355,689	13		13	Other endemic	13,850	3,614	Yes	Clin.Def
Burkina Faso*	489,026	34%	322,757	2	1	3	High risk	12,471	1,606	Yes	Clin.Def
Cameroon*	541,891	48%	281,783	0	2	2	High risk	10,498	1,475	Yes	Clin.Def
Madagascar*	560,345	57%	240,948	0	0	0	High risk	5,986	1,336		Sub-Clin.Def.
Mali*	456,013	48%	237,127	1		1	High risk	12,438	2,390	Yes	Clin.Def
Myanmar	868,114	73%	234,391	1	13	14	High risk	6,305	1,205		Sub-Clin.Def.
Tanzania*	1,241,600	82%	223,488	2	6	8	High risk	9,503	933	Yes	Clin.Def
Yemen	769,340	72%	215,415	2	22	24	High risk	7,175	2,339		Clin.Def
Chad	293,431	33%	196,599	23	3	26	Other endemic	6,110	2,517	Yes	Clin.Def
Kenya*	929,175	79%	195,127	1	5	6	High risk	22,051	1,074	Yes	Clin.Def
Ghana*	690,599	72%	193,368	12	1	13	Other endemic	17,964	1,932	Yes	Clin.Def
Côte d'Ivoire*	500,068	64%	180,024	3	2	5	Other endemic	3,728	1,135	Yes	Sub-Clin.Def.

KEY: **Clin.Def**: Clinical deficiency. **Insuf.Dat/Lik**: Insufficient data but deficiency likely. **Sub-Clin.Def:** Sub-clinical deficiency

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* Approved for support from The Vaccine Fund.

Vaccine Fund countries				Polio staff			Polio free	Measles (1997)	MNT (1998)	Yellow fever	Vitamin A
	Surviving Infants	DPT3 Coverage	Unimmunized population	International	National	Total	Risk	Deaths 0-4 years of age	Estimated deaths	Endemic countries	Status
Nepal	731,976	76%	175,674	6	33	39	Other endemic	6,016	2,935		Clin.Def
Senegal	347,476	52%	166,788	1		1	High risk	3,197	2,281	YF	Sub-Clin.Def.
Mozambique*	736,335	81%	139,904	1		1	High risk	6,995	3,018		Clin.Def
Guinea	275,930	57%	118,650	2		2	High risk	9,344	1,258	YF	Clin.Def
Sudan	891,322	87%	115,872	23	233	256	Priority	5,605	2,209	YF	Clin.Def
Cambodia*	320,461	64%	115,366	1		1	Certified polio-free	1,724	1,472		Clin.Def
Viet Nam	1,580,879	93%	110,662	1		1	Certified polio-free	4,018	532		Sub-Clin.Def.
Liberia*	129,090	23%	99,399	3	4	7	High risk	3,756	638	YF	Clin.Def
Haiti*	240,272	59%	98,512			0	Certified polio-free	23	75	YF	Insuf.Dat/Lik
Burundi	244,252	63%	90,373	1		1	High risk	4,712	730	YF	Sub-Clin.Def.
Togo	172,524	48%	89,712	1		1	High risk	5,557	278	YF	Clin.Def
Lao DPR*	189,341	56%	83,310	1		1	Certified polio-free	1,421	417		Clin.Def
Congo	114,307	29%	81,158	4	16	20	Other endemic	2,387	48	YF	Sub-Clin.Def.
Sierra Leone*	183,827	56%	80,884	6		6	Other endemic	2,010	793	YF	Sub-Clin.Def.
Mauritania	96,713	19%	78,338	0	1	1	High risk	2,298	236	YF	Clin.Def
Malawi*	437,677	83%	74,405	1		1	High risk	1,289	852		Clin.Def
Central Af. Rep.	120,924	45%	66,508	3	5	8	Other endemic	2,381	201	YF	Insuf.Dat/Lik
Zimbabwe	330,520	81%	62,799		1	1	High risk	8,437	206		Clin.Def
Papua New Guinea	141,665	56%	62,333	1		1	Certified polio-free	1,268	396		Sub-Clin.Def.
Eritrea	137,447	56%	60,477		2	2	High risk	3,515	592	YF	Sub-Clin.Def.
DPR Korea	447,015	87%	58,112	2		2	High risk	29			Insuf.Dat/Lik
Guinea-Bissau	43,656	6%	41,037	2		2	High risk	1,161	129	YF	Insuf.Dat/Lik
Rwanda*	272,015	85%	40,802	0	0	0	High risk	5,247	141	YF	Clin.Def
Tajikistan*	176,526	<80%	35,305			0	High risk	14			Insuf.Dat/Lik
Nicaragua	168,358	83%	28,621	1		1	Certified polio-free	7		YF	Sub-Clin.Def.

* Approved for support from The Vaccine Fund.

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Vaccine Fund countries				Polio staff			Polio free	Measles (1997)	MNT (1998)	Yellow fever	Vitamin A
	Surviving Infants	DPT3 Coverage	Unimmunized population	International	National	Total	Risk	Deaths 0-4 years of age	Estimated deaths	Endemic countries	Status
Zambia	351,726	92%	28,138	1	5	6	High risk	1,332	218		Clin.Def
Lesotho	67,675	64%	24,363			0	Low risk	601			Sub-Clin.Def.
Benin	225,698	90%	22,570	4	1	5	Other endemic	2,898	99	YF	Clin.Def
Djibouti	20,784	23%	16,004	1		1	High risk	252			Sub-Clin.Def
Bhutan*	72,550	86%	10,157			0	Low risk	191			Clin.Def
Bolivia	249,606	96%	9,984	2		2	Certified polio-free	12		YF	Sub-Clin.Def.
Honduras	198,928	95%	9,946			0	Certified polio-free	10		YF	
Azerbaidjan*	117,046	93%	8,193			0	Polio free	9			Insuf.Dat/Lik.
Cuba	136,068	94%	8,164			0	Certified polio-free	1		YF	
Georgia	67,170	89%	7,389			0	Polio free	64			Insuf.Dat/Lik.
Uzbekistan	625,350	99%	6,254			0	High risk	210			Clin.Def
Comoros	23,105	75%	5,776			0	Low risk	518	47		Clin-Def
Mongolia	54,880	90%	5,488			0	Certified polio-free	7			Clin-Def
Ukraine	473,606	99%	4,736			0	Polio free	44			Insuf.Dat/Lik.
Gambia	44,873	90%	4,487	1		1	High risk	292		YF	Sub-Clin.Def
Armenia*	45,485	91%	4,094			0	Polio free	8			
Bosnia & Herzegovia	40,516	90%	4,052			0	Polio free	19			Insuf.Dat/Lik.
Sri Lanka	323,436	99%	3,234			0	High risk	428			Clin.Def
Guyana*	16,397	83%	2,787			0	Certified polio-free	1		YF	Sub-Clin.Def
Turkmenistan	113,506	98%	2,270			0	High risk	17			Insuf.Dat/Lik.
Solomon Islands	14,880	86%	2,083			0	Certified polio-free	16			Clin-Def
Albania	58,326	97%	1,750			0	Polio free	16			Insuf.Dat/Lik.
Moldova	54,366	97%	1,631			0	Polio free	4			Insuf.Dat/Lik.
Kyrgystan*	109,752	99%	1,098			0	Polio free	17			Insuf.Dat/Lik.
Sao Tome*		73%				0	Low risk	103		YF	
TOTAL				**285**	**1162**	**1447**					

* Approved for support from The Vaccine Fund.

Appendix 3 to Annex 6.2:
Summary map of immunization initiatives

(draft dated 12 June 2001)

OBJECTIVES	
GAVI	**(1) Improve access to sustainable immunization services.** (2) Expand the use of all existing safe and cost-effective vaccines. (3) Accelerate the development and introduction of new vaccines. (4) Accelerate research and development efforts for vaccines and related products specifically needed by developing countries, particularly vaccines against HIV/AIDS, malaria and TB. (5) Make immunization coverage a centrepiece in the design and assessment of international development efforts. • GAVI underwrites goals and objectives of **WHA and WSC 1990** in particular **polio eradication and reduction of measles mortality and morbidity** (Proto-Board Doc July 1999, pg.8) • The Board reaffirmed its previously stated objective to **reduce measles mortality**: "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**." (GAVI Board Meeting, 19 Nov.2000; pg.4)
Polio	Global eradication of poliomyelitis by the year 2000, to be pursued in ways which "**strengthen the development of immunization programmes as a whole**, fostering its contribution in turn, to the development of the health infrastructure and of primary health care". (WHA41.28;1988)
Measles	(1) **To halve the annual number of measles deaths by 2005 relative to 1999 estimates.** (2) To achieve and maintain interruption of indigenous measles transmission in large geographical areas with established elimination goals (Americas by 2000; Europe by 2007; Mediterranean by 2010). (3) To convene a global consultation in 2005, in collaboration with other major partners, to review the progress and assess the feasibility of global measles eradication. /...

KEY:

Bold text = similarities

Bold, underlined text = differences

OBJECTIVES *(continued)*	
Vitamin A	By 2000, the virtual elimination of vitamin A deficiency (VAD) and its consequences, including blindness (WSC 1990).
MNT	By 2005, the elimination of maternal and neonatal tetanus as measured by the reduction of NT cases to fewer than 1 case per 1,000 live births in every district of every country.
Yellow fever	By the year 2005: • 80% of countries at risk would have integrated YF into **routine immunization** and will achieve 80% yellow fever coverage. • All countries at risk will be conducting case-based surveillance and reporting suspected yellow fever cases, with laboratory results. • **Catch-up campaigns** achieving at least 80% coverage will be undertaken in high-risk districts (given vaccine availability).

Milestones

GAVI

(1) **By 2005, 80% of developing countries should have routine immunization coverage of at least 80% in all districts (e.g., as measured by DTP3 and measles).**

(2) By 2002, 80% of all countries with adequate delivery systems should have introduced HepB vaccine; by 2007 this should have been achieved in all countries.

(3) By 2005, 50% of the poorest countries with high disease burdens and adequate delivery systems should have introduced Hib vaccine.

(4) By 2005 the vaccine efficacy and disease burden in respect of rotavirus and pneumococcal disease should be known for all regions, and a mechanism should have been identified to make the vaccines available for the poorest countries.

(5) During 2000...analysis of benefit, market and policy failure in R&D and commercialization of candidate vaccines for HIV/AIDS, malaria and TB...make recommendations to overcome problems.

Polio

(1) By end of 2001, a maximum of 10 countries will be polio-endemic and certification-standard surveillance will be achieved by all endemic and recently-endemic countries.

(2) By the end of 2002, poliovirus transmission will be interrupted globally and the containment process will have begun in all WHO regions.

(3) By the end of 2003, global wild poliovirus final repositories will be indentified.

(4) By the end of 2004, a consensus strategy will be developed to stop polio immunization.

(5) By the end of 2005, global certification of poliomyelitis eradication will be achieved, and routine immunization systems will be strengthened with a targeted coverage of 80% in 80% districts globally.

Measles

(1) By end of 2001, the Global Strategic Plan to be finalized and endorsed by partners; All regions to review and update where appropriate their measles control and elimination plans in accordance with the Global Strategic Plan; All countries with the highest measles mortality and/or in the high mortality strata to have developed a 3-5 year strategic plan for achieving and sustaining measles mortality reduction targets; interruption of measles transmission to be achieved and maintained in the Region of the Americas.

(2) By the end of 2002, all countries with the highest measles mortality and/or in the high child mortality strata to have begun accelerated activities for achieving and sustaining the measles mortality reduction targets.

(3) By the end of 2003, annual global measles mortality to have been reduced by a third relative to 1999 estimates.

(4) By the end of 2004, countries with high measles mortality to have administered at least one dose of measles vaccine to at least 90% of children aged 9 months to 4 years, in a strategy that will be sustained over time (**routine** or **supplemental**). /...

Milestones *(continued)*	
Measles *(cont)*	(5) By the end of 2005, annual global measles mortality to have been reduced by half relative to 1999 estimates; WHO and UNICEF, in collaboration with CDC and other major partners, to convene a global meeting in order to review progress towards achieving the targets for mortality reduction and regional elimination and assess the feasibility of global measles eradication.
Vitamin A	By end 2000, all countries where populations are affected by VAD or likely to be affected (based on infant and child mortality criteria) should at a minimum have a detailed plan of action for elimination of vitamin A deficiency as a public health problem, with a resource mobilization and allocation plan to support actions. By mid-year 2002, all of these countries should have activities and monitoring systems in place and should have data on process indicators corresponding to key programme strategies. By end 2005, all affected countries should have assesses or re-assessed vitamin A deficiency through nationally representative surveys using serum retinol or other more convenient criteria that may be better established at that time.
MNT	By 2005, the elimination of maternal and neonatal tetanus as measured by the reduction of NT cases to fewer than 1 case per 1,000 live births in every district of every country.
Yellow fever	-

Policy context	
GAVI	GAVI Proto-Board Report (July 1999); Immunize Every Child (Feb. 2000) **WSC 1990** **WHA resolutions** **UNGASS 2001**
POLIO	**WHA – May 1988** **WSC – 1990** Polio Strategic Plan 2001-2005 **UNGASS 2001**
Measles	**WHA – 1989** **WSC – 1990**
Vitamin A	Vitamin A Global Initiative: A Strategy for Acceleration of Progress in Combating Vitamin A Deficiency. **WSC – 1990** **WHA – 1991** Internationall Conference on Nutrition - 1992 **UNGASS – 2001**
MNT	**WHA – 1989** **WSC – 1990** **UNGASS – 2001**
Yellow fever	Joint WHO/UNICEF Technical Group on Immunizations in Africa (1988) Yellow fever – Technical Consensus Meeting (March 1998) Control of yellow fever in the African Region 1999-2001: Three-Year Plan of Action (WHO 1998)

Key partners	
GAVI	• Board Members: **Bill & Melinda Gates Foundation; WHO; UNICEF; The World Bank** • Rotating Board Members: Rockefeller Fdn;CVP;**CDC**; NIH (US); CIGB; **Aventis Pasteur; Canada; Netherlands; Norway**; Bhutan; Mali. • Others: **USAID, IFMPA**
Polio	Rotary International; **WHO; UNICEF; CDC; Bill & Melinda Gates Foundation**; UNF; OPEC; **Aventis Pasteur**; Debeers; **IFPMA**; EU; **World Bank; Micronutrient Initiative; USAID**; Japan; Denmark; Netherlands; **Canada**; Belgium; Australia; Malaysia; **Norway**; Portugal; Republic of Korea; Switzerland; UAE; Finland; Italy; Smith-Kline Biologicals; Institute Merieux; Ms. Martina Hingis; Custom Monoclonals International.
Measles	**WHO; UNICEF; CDC**; American Red Cross; DFID; CIDA
Vitamin A	Global Vitamin A Initiative (GAVI) – **UNICEF; WHO; USAID; CIDA; Micronutrient Initiative (Canada); Canada, the Netherlands**, Japan, United Kingdom, United States, MOST, IVACG. Others: Helen Keller International, Sight and Life, Industry, UNF.
MNT	**UNICEF; WHO**; UNFPA; **Bill & Melinda Gates Foundation**; Becton-Dickson; Japan; Ronald MacDonald House.
Yellow fever	**WHO; UNICEF; CVP; GAVI/GFCV; AMP**.

Strategies/activities	
GAVI	• Global: Advocacy;Country-Coordination; Financing; R&D • National: (1) Procurement of hepB, Hib and YF vaccines and safe immunization materials. (2) **Immunization services infrastructure support.** • Requirements: **ICC**; recent assessment of immunization services; **multi-year plan.** Note: Performance/outcome-based grant approach; "bottom-up" proposal process.
Polio	(1) **High routine infant immunization coverage with OPV.** (2) **National immunization days (NIDs).** (3) AFP **surveillance** and laboratory investigation. (4) **Mop-up campaigns (house-to-house).** (5) **Combine vitamin A supplementation with OPV in areas where vitamin A deficiency is prevalent.** Process: (1) **ICCs** (2) **Micro-planning** (3) Social mobilization (4) Advocacy
Measles	(1) **Routine immunization achieving at least 90% routine vaccination coverage (in each district and nationally) with at least one dose of measles vaccine at nine months or shortly thereafter.** (2) Provision of a second opportunity for measles vaccination for all children through **routine** or **supplemental** activities. (3) Establishing effective measles **surveillance.** (4) **Improved management of complicated cases, including vitamin A.** (5) **Combine vitamin A supplementation with measles vaccination in areas where vitamin A deficiency is prevalent.**
Vitamin A	(1) **Vitamin A supplementation every 4-6 months to children under-five years living in VAD areas (opportunity to link to immunization campaigns and routine immunization services).** (2) Vitamin A supplementation once to post-partum mothers (**also can be linked with first immunization contact**) in VAD areas. (3) Dietary diversification. (4) Food fortification. /...

Strategies/activities *(continued)*	
MNT	(1) **Immunization campaigns targeting high-risk and hard to reach areas.** (2) Promotion of clean delivery practices. (3) **Sustain elimination by high routine TT coverage for pregnant women and routine DTP coverage for children.** (4) MNT **surveillance**.
Yellow fever	(1) **Prevention through routine immunization** and **preventive mass immunization "catch-up" campaigns.** (2) Strengthening of **surveillance** including laboratory capacity to confirm suspect cases. (3) Strengthening of outbreak response through Inter-country planning and improved epidemic preparedness. (4) Ensuring sustainable vaccine supply.

Key indicators	
GAVI	DTP3 and measles (as per first milestone).
Polio	AFP rates of 1/100,000 under 15 years.
Measles	Measles vaccine coverage; number of countries providing second dose.
Vitamin A	Vitamin A coverage; number of vitamin A deficient countries adding vitamin A to routine EPI.
MNT	Less than 1 case per 1,000 live births in every district of every country.
Yellow fever	Yellow fever vaccine coverage; % of endemic countries where YF coverage = measles coverage.

Institutional arrangements	
GAVI	Regional Working Groups; TFCC.
Polio	ICC, TCG, Labnet, Surveillance, SAGE; BBC/VOA/RFI.
Measles	Steering Committee on Research Related to Measles Vaccines and Vaccination.
Vitamin A	-
MNT	-
Yellow fever	-

Geographic focus	
GAVI	74 eligible countries (GNP <US$1000).
Polio	Endemic: 20 countries; Recently endemic/high-risk: 35 countries; Low-risk: 76 countries; Certified polio-free: 84 countries.
Measles	DRC, Ethiopia, India, Nigeria account for 50% of estimated global measles mortality.
Vitamin A	136 countries where VAD is a public health problem (93 countries with data; data lacking for 43 countries but VAD very likely); 140-250 million children under five at risk.
MNT	57 countries.
Yellow fever	34 countries "at risk" in Africa; 11 countries in PAHO.

Mortality Impact	
GAVI	Reduce 2.6 million annual VPD deaths by ?
Polio	3 million children walking.
Measles	888,000 measles deaths per year; 30 million measles cases per year.
Vitamin A	23% reduction in *all cause* childhood mortality in VAD areas; 50% reduction in measles mortality when vitamin A given as treatment; Between 650,000 to 1 million child deaths averted since 1998.
MNT	215,000 neonatal deaths per year (1998) (14% of total); 30,000 maternal deaths annually (1993) (5% of total).
Yellow fever	Estimated 200,000 yellow fever cases with 30,000 deaths each year (mostly in sub-Saharan Africa).

Estimated per unit cost	
GAVI	US$20 per child incentive.
Polio	US$0.50 per child/NIDs round; OPV – US$0.09.
Measles	US$1 per child vaccinated ($0.26 for vaccine/syringe/safety box costs).
Vitamin A	US$0.10 per child/NIDs round (incremental cost when given with OPV); US$0.43 per child (when given as Vitamin A Campaign alone); Vitamin A capsules – US$0.02.
MNT	US$1.20 per woman (includes 3 doses safely given; operational costs; promotion of clean deliveries).
Yellow fever	US$0.39 yellow fever vaccine in 2001 (to increase to US$0.48 in 2003)(UNICEF prices); Estimated cost to add yellow fever to routine EPI was US$0.83 per child.

	Total funding required
GAVI	US$1.75 billion over five years (2001-05).
Polio	US$1 billion over five years (2001-05).
Measles	US$1 billion over five years.
Vitamin A	US$90 million cost of capsules only over five years.
MNT	US$130 million over five years (2001-05).
Yellow fever	Total: US$180 million over five years (Catch-up campaigns US$75 million).

Resources available	
GAVI	Financial: Currently US$1 billion over five years (2001-2005); Approved 2001-2005 (to date) – US$375 million to 25 countries (73% new vaccines US$272 million; 27% infrastructure US$103 million); Staff: GAVI Secretariat five professionals; two support staff.
Polio	Financial: US$600 million over five years (pledged or committed); WHO staff: 1555 (316 international; 1239 national); WHO vehicles: >1000; Cold chain: being collected; Laboratory network: 148 laboratories; Institutional arrangements: see above (for polio).
Measles	Financial: currently US$20 million; (CDC US$10 million; UNF US$5 million; ARC US$5 million) additional contributions from CDC and other partners currently being discussed.
Vitamin A	Financial: currently US$30 million for capsules over five years (MI/CIDA); UNICEF: US$6 million/year for operational costs; WHO: US$1 million/year for operational/technical support costs.
MNT	Financial UNICEF: US$60 million (US$26 million from Bill & Melinda Gates Foundation plus US$24 million from others (note: US$22 million "in kind"); Financial national governments: US$30 million expected; Staff UNICEF: two professionals NY; country staff?
Yellow fever	Financial WHO: US$1million over 2 years (2000-2001) (CVP – West Africa) (AMP); GAVI to pay for some activities (vaccine/routine) in eligible countries.

Funding shortfall	
GAVI	US$750 million over five years (2001-05).
Polio	US$400 million over five years (2001-2005); (US$225 million of which is required during 2001-2002).
Measles	US$1 billion over five years.
Vitamin A	US$60 million shortfall for capsules; US$?? Operational/technical support costs; GAVI to pay for some activities (vaccine/routine) in eligible countries.
MNT	US$40 million over 5 years (2001-05).
Yellow fever	US$180 million (minus approximately US$70 million of vaccine provided through GFCV).

Appendix 4 to Annex 6.2: Summary analysis of alignment scenarios *(draft dated 11 May 2001)*

Scenario	Implications			
	Advocacy	**Fund-raising**	**Coordination**	**Country operations**
#1. Status quo	**Negative** • GAVI message missing a big ADC impact. • GAVI mission perceived as incomplete.	**Positive** • Separate initiatives and fund-raising efforts results in overall higher fundingfor childhood immunization.	**Negative** • Ministries and donors approached by ADC initiatives and GAVI from different levels (Regional/HQ), at different times, by different contact points.	**Negative** • Friction as GAVI processes (assessment, multi-year plan, ICC) largely implemented by 350 ADC-funded international staff and physical infrastructure.
#2. Adopting new objective/ milestone and indicators	**Positive** • GAVI advocacy enhanced by aligning with leading "killers" and high profile initiatives.	**Positive** • As above.	**Negative** • As above (although slight improvement at regional level engaged in monitoring and evaluation).	**Negative** • As above (although less disconnect between GAVI processes, national VPD priorities, and activities eligible for Fund support).
3. New objective, milestone/ indicators and cost sharing	**Positive** • Facilitates role of ADC stakeholders in GAVI advocacy efforts.	**Positive** • As above, but stronger GAVI/ADC linkages more appealing to donors.	**Positive** • Vaccine Fund support, particularly personnel, would compel coordination at all levels.	**Positive/Negative** • Country staff receive consistent priorities with enhanced opportunities for implementing ADC lessons. • Countries still have problem of separate funding streams.
4. Full integration of processes and funding	**Positive** • As above (increased credibility of GAVI as "New EPI").	**Negative** • Generally felt that combined fund-raising efforts would overall raise less money.	**Positive** • GAVI financial role forces coordination through institutional arrangements (ICCs, TCG, etc) and fully engages regional level.	**Positive** • As above, integrated funding harmonizes activities from country perspective.

Annex 7
Update on project agendas of the GAVI Task Force on R&D

Annex 7.1: Short summary of a meeting (Bethesda, April 2001) convened to prepare a global agenda to expedite development and introduction of pneumococcal conjugate vaccines
(Prepared by Orin Levine)

Annex 7.2: Summary of the pneumococcal conjugate vaccine global agenda for accelerated development and introduction, including identification of highest level priorities
(Prepared by Orin Levine, Thomas Cherian, Jay Wenger)

Annex 7.3: Preliminary draft of recommendations from the meeting (Geneva, May 2001) convened to begin preparing a global agenda for accelerated development and introduction of rotavirus vaccines into developing countries
(Prepared by Joe Bresee, Roger Glass and Bernard Ivanoff)

Annex 7.4: Summary of a Workshop of the GAVI Task Force on Research and Development, Bethesda, April 2001, on "New vaccine technologies"
(Prepared by Peter Wilson)

Annex 7.5: A proposed step-wise way forward to select "vaccine technologies" for accelerated development and introduction
(Prepared by Teresa Aguado and Uli Fruth)

Annex 7.6: Summary of the meningococcal A/C conjugate vaccine project
(Prepared by Luis Jodar and Regina Rabinovich)

Annex 7.1
Summary of progress on the pneumococcal conjugate vaccine agenda

Meeting, Bethesda, Maryland, 19-20 April 2001

The GAVI Task Force on Research and Development (R&D), with NIAID as host partner, recently held a meeting in Bethesda, MD to determine the activities in the area of R &D that will be needed to achieve this objective. This meeting was designed to be one part of a process to develop a broad agenda of activities to accelerate the uptake of pneumococcal conjugate vaccines in developing countries – a process that is involving all four GAVI task forces. It was also designed to be a focused meeting – that is a meeting where the discussion should be focused on R&D-related activities needed to address the objective of accelerating pneumococcal conjugate vaccine introduction in developing countries. As such, it was not in any way meant to be a meeting to discuss the breadth of research needed in pneumococcal disease and pneumococcal vaccination generally. There are many important activities related to improving our understanding of pneumococci, pneumococcal disease, and pneumococcal vaccines that are clearly important areas for research, but were not appropriate for discussion at this particular meeting.

The meeting included approximately 40 participants representing the secretariat of the GAVI Task Force on R&D, technical agencies, academia, regulatory agencies, and industry. Participants represented virtually all regions of the globe. The meeting focused on assessing the key activities in R&D that will provide the basis for introduction of pneumococcal conjugate vaccines into EPI globally. As a starting point, the meeting considered an existing list of priority activities that had been developed just over two years previously at a WHO meeting in Geneva. Since that time tremendous changes have occurred in immunization generally (e.g., the formation of GAVI, the creation of The Vaccine Fund) and in pneumococcal conjugate vaccination specifically (e.g., the licensure of a 7-valent pneumococcal conjugate vaccine for use in the US and Europe). The meeting reviewed the existing priority list and made recommendations for changes based on the recent developments. At the last session of the meeting, members of the community submitted suggestions to the TF on how to move forward from the meeting to make the agenda as successful as possible. In general the suggestions were focused on maintaining a high degree of transparency in the process and reaching out to include the many key people who were not at the meeting but who play a critical role to accomplishing the objectives.

The meeting did not provide enough time to rank each individual priority activity and the participants asked to be able to review the draft activity list and assign priorities. We are currently in that follow-up period. The meeting participants received a rough draft of the priority activities that were discussed on 25 April and were asked to rank the activities and provide comments on the individual activities by 9 May. We are currently at the point of collating and organizing all of the revisions. At that point we will consider the need for additional rounds of distribution but the group at the meeting urged us to move rapidly to disseminate the document for wider consumption as soon as possible. We expect to have a revised document completed by mid-June.

We are planning to actively disseminate the revised document by e-mail to a broad range of members of the pneumococcal R&D community. We are also planning to make it available on the GAVI website on a page devoted to the activities of the Task Force on R&D.

Annex 7.2
R&D activities necessary to accelerate introduction of pneumococcal conjugate vaccine use in developing countries

Report from a meeting sponsored by the GAVI Task Force on R&D, held at the US National Institutes of Health, Bethesda, MD, April 19-20, 2001

Summary of the report

The objective of the meeting was to define a limited set of high priority activities that will be needed to help accelerate the evaluation and introduction of pneumococcal conjugate vaccines for routine infant immunization in developing countries. Several areas of work important for achieving this goal were highlighted. This document is organized into the six general areas of high priority activity that were identified:

A. development of methods to estimate the spectrum of disease burden in different settings;

B. collection of disease burden data for key outcomes;

C. expanded evaluation of the overall impact of routine immunization in developing country settings;

D. generation of greater local advocacy from research efforts;

E. evaluation of alternative regimens better suited to developing countries; and

F. establishment of methods and materials to facilitate licensure of pneumococcal vaccines.

Each section includes a brief paragraph describing the background and rationale for making the activities a key priority. Activities were assigned to one of three priority levels based on importance, urgency, and relationship to antecedent activities. Priority level 1 corresponds to very important and urgently needed; priority level 2 corresponds to important but less urgent; and priority level 3 includes activities whose conduct is influenced by antecedent activities. Among the 17 priority activities that were identified, 6 were highlighted as both highest priority and urgently needed (these are indicated in the text by **bold lettering**). The 6 activities identified as priority level 1 (important and urgent) are:

- developing a range of methods to assess key disease-burden measures in different settings;
- standardizing diagnosis of pneumonia by chest x-ray;
- expanding surveillance for laboratory confirmed pneumococcal disease
- measuring the burden of pneumonia;
- establishing long-term surveillance to evaluate the impact of immunization;
- generating more local advocacy and ownership from existing and future research efforts.

The activities listed in this document represent activities focused on achieving a substantial but narrow objective – accelerating the introduction of pneumococcal conjugate vaccines

into infant immunization programmes in developing countries. As such, this document is not by any means a comprehensive listing of all valuable research on pneumococci, pneumococcal diseases, and pneumococcal vaccination. The broader goals of a more comprehensive understanding of pneumococcal diseases and the prevention and treatment of pneumococcal infections in all ages and in all countries will clearly require efforts beyond the narrow focus of this document.

This document is intended to serve several functions. First, it is hoped that it will be used by individuals and groups to advocate for support for their own efforts to accelerate the introduction of pneumococcal conjugate vaccines. Second, this document can serve as a useful tool for coordinating the activities of the many partners involved in this process. Finally, the document can be used as a management tool by international agencies to track progress to the achievement of the key activities needed to accelerate pneumococcal conjugate vaccination, and as useful guide to help them with their own decisions about how to use resources.

Neither the GAVI secretariat nor The Vaccine Fund currently have funds to support the activities outlined in this document. Success in realizing the activities outlined here will depend on the ability of the research and public health community to promote the importance of this effort and to obtain the needed resources.

A. Developing methods to estimate the burden of pneumococcal disease in developing countries

A.1 Developing a range of methods to assess key disease-burden measures in different settings (Priority level 1)

Rationale: Demonstrating the local burden of disease is an essential, primary step in the process of introducing a new vaccine. The overall burden of pneumococcal disease, however, is not well-defined in most regions. Unfortunately, not all existing methods for defining disease burden are equally robust in all regions of the world, and for some key outcomes, such as pneumonia and otitis media, improved methods are needed. Ultimately, countries will need to have a menu of key outcomes with alternative methods to measure them, from which they can choose the most appropriate to local conditions and resources.

Activity: A working group should develop a set of various methods for defining the burden of pneumococcal disease and for monitoring the overall impact of pneumococcal conjugate vaccination. Based on the success of the WHO-organized Pneumococcal Trialists Group and the Colonization Working Group, it is appropriate for WHO to be the GAVI partner responsible for this activity. The goal for this working group should be to develop a menu of alternative methods (from complex, very precise, and expensive to simple, less precise, and less expensive) for measuring or estimating a variety of outcomes (e.g., overall mortality, pneumonia mortality, x-ray confirmed pneumonia, clinically diagnosed pneumonia, meningitis, chronic otitis, hearing loss) that may be due to pneumococcal infection. This "menu of options" will allow countries to match the methods and endpoints most appropriate to local priorities and resources.

A.2 Standardizing diagnosis of pneumonia by chest x-ray (Priority level 1)

Rationale: Pneumonia is the most common form of severe pneumococcal disease. Most patients with pneumococcal pneumonia will have evidence of pneumonia on chest x-ray but will not have a positive blood culture. Interpretation of chest x-rays, however, is complicated and prone to vary between interpreters. In the absence of standardization, it is difficult to compare the results of vaccine trials and surveillance studies that use radiographic pneu-

monia as an endpoint. Standardization of definitions and interpretation of a radiographic pneumonia endpoint will greatly improve the ability to determine the burden of pneumonia preventable by pneumococcal vaccination.

Activity: Building on the process and definitions developed by the WHO pneumococcal vaccine trialists working group, a training programme for standardizing the interpretation of chest x-rays to diagnose pneumonia needs to be developed and made available to individuals who are interested in carrying out surveillance for radiographically-confirmed pneumonia.

B. Expanding efforts to collect pneumococcal disease burden data

B.1 Expanding surveillance for laboratory confirmed pneumococcal disease (Priority level 1)

Rationale: Many countries do not perceive pneumococcal disease as a major problem in childhood because they rarely isolate the pathogen from specimens of blood or CSF. While surveillance based on isolates from blood and cerebrospinal fluid (CSF) will only detect a small fraction of the overall burden of pneumococcal disease in a population, it can provide several important pieces of information:

1) tangible evidence that *S. pneumoniae* causes disease in the local population;

2) estimates of the most common serotypes and their antibiotic susceptibility patterns; and

3) a highly specific indicator for monitoring the impact of vaccination if it is introduced.

When organized into regional or sub-regional networks using standard methods, the surveillance data is likely to be more consistent and to generate more advocacy as a result. In many countries the lack of laboratory capacity is a major obstacle to the successful conduct of invasive disease surveillance.

Activity: Establish regional/sub-regional networks of sentinel sites for surveillance of invasive disease. This will include the need to improve the capacity of local laboratories to isolate *S. pneumoniae* from blood and CSF specimens and to apply standard epidemiologic surveillance methods in all the sites.

B.2 Measuring the burden of pneumonia (Priority level 1)

Rationale: In every region, pneumonia is perceived as an important child health problem and yet few areas have accurate data on the local burden of childhood pneumonia. Pneumonia is the most common presentation of severe pneumococcal disease; however, the yield from blood cultures in pneumonia patients is low so culture-based methods do not accurately measure the true burden of pneumococcal pneumonia. Clinical trials that assess the reduction in the incidence of clinically or radiographically-diagnosed pneumonia are the most accurate measures of the amount of pneumonia preventable by pneumococcal vaccination. Clinical trials, however, will only be conducted in a handful of settings. A method for measuring the incidence of pneumonia that can be used in countries that are not doing clinical trials is needed. This method should be similar to that used in the clinical trials so that it can serve as a "bridge" between the results from clinical trials and the local surveillance data.

Activity: Establish surveillance using the recently developed generic protocol for surveillance to estimate the incidence of pneumonia in 3-6 sites. Preferably these sites should represent a broad range of environments and health care settings, and should compare the results of surveillance based on x-ray diagnosis with that obtained by clinical diagnosis of pneumonia. Based on the experience in the field tests the protocol should be revised and the use of the protocol expanded to a larger number of field sites as soon as possible.

B.3 Evaluating the key disease burden outcomes in each region (Priority level 2)

Rationale: Perception of the disease outcomes that are critical for evaluating the utility of pneumococcal vaccines may vary in different regions and in different countries (e.g., overall mortality may be perceived as the key outcome in an African country like Chad versus pneumonia hospitalizations in a South American country like Chile). Additional information on the outcomes that are perceived as critical for the evidence base to evaluate the introduction of pneumococcal vaccines will help to guide efforts to collect the most appropriate data.

Activity: Survey regional and national opinion leaders to determine the key disease outcomes of importance in their region/country (e.g., overall mortality, chronic otitis media, hearing loss, antibiotic resistance).

B.4 Establishing the economic impact of pneumococcal disease and the potential cost-effectiveness of immunization (Priority level 2)

Rationale: The economic burden of pneumococcal disease, including antibiotic resistance, is not well established. Consequently, countries may not assign much value to a pneumococcal conjugate vaccine. Further efforts to estimate the costs associated with pneumococcal disease will provide important information for decision-makers who must weigh the costs of immunization against the costs of the disease.

Activity: Make additional efforts to estimate accurately the economic burden of pneumococcal disease in different regions. This effort should begin with the evaluation of the cost-effectiveness of pneumococcal vaccination in the context of ongoing pneumococcal conjugate vaccine trials in developing countries. Adaptation of the methods to be appropriate to non-trial sites will be important.

C. Assessing the efficacy, effectiveness, and safety of pneumococcal conjugate vaccination in developing countries

C.1 Establishing long-term surveillance to evaluate the impact of immunization (Priority level 1)

Rationale: Routine vaccination may lead to unexpected positive and negative effects – herd immunity and serotype replacement disease – that may only become apparent after sustained use of the vaccine and may only be detected by careful surveillance for key pneumococcal disease outcomes, e.g., invasive disease and pneumonia. Populations currently participating in efficacy trials and high-risk populations of industrialized countries, where extensive baseline surveillance exists, represent unique opportunities to address these critical issues. Information on herd immunity will inform decisions about the need for alternative strategies for prevention of disease in very young infants (e.g. <3 months old).

Activity: Support continued surveillance for invasive disease and, if possible, nasopharyngeal colonization, in populations where efficacy studies have been or are being conducted (e.g., South Africa, the Gambia, Philippines) and in high-incidence sub-populations of industrialized countries where routine immunization has been introduced and baseline (pre-vaccination) surveillance data are available (e.g., Australian Aboriginals, Native North Americans in the USA and Canada). These sites should monitor three issues:

1) long-term impact of vaccination on invasive disease caused by vaccine serotypes;

2) the possible emergence of serotype replacement; and

3) the possible occurrence of herd immunity effects (i.e., reductions in the incidence of vaccine-serotype disease among unimmunized populations).

C.2 Establishing the efficacy/effectiveness of pneumococcal conjugate vaccination against key endpoints in developing countries (Priority level 2)

Rationale: There are several examples illustrating that one cannot simply extrapolate the results from studies in industrialized countries (where mortality from pneumococcal disease is rare, access to care is good, and co-morbidities are uncommon) establishing the efficacy of vaccines against mild disease endpoints to moderate and high mortality countries, where more severe disease endpoints are important. Data are needed on the effectiveness of vaccination for protecting against key outcomes that may not have been evaluated in studies in industrialized countries (e.g., all-cause mortality, pneumonia mortality, radiographic pneumonia). Where possible, these studies should monitor the impact on invasive pneumococcal disease to assess the occurrence of possible herd immunity effects and/or serotype replacement (i.e., increases in invasive disease due to serotypes not included in the conjugate vaccine). Additional efficacy/effectiveness data for specific outcomes (e.g. chronic otitis, mortality, hospitalizations, ER visits) may be required for certain regions. Surveillance for colonization may provide important information related to changes in the serotype distribution as a consequence of routine immunization, and should be considered if sufficient resources are available.

Activity: Continue support of ongoing efficacy studies in developing countries and conduct demonstration projects to assess the effectiveness of pneumococcal conjugate vaccination in non-industrialized settings and to measure the disease burden preventable by routine pneumococcal conjugate vaccination. These projects are most needed in regions that represent distinct populations and where there are no ongoing efficacy trials and/or where the burden of disease is not well-defined (e.g., China, the Indian sub-continent, and the commonwealth of independent states [CIS] of eastern Europe).

D. Generating more local advocacy from research efforts

D.1 Generating more local advocacy and ownership from existing and future research efforts (Priority level 1)

Rationale: Experience with Hib vaccine introduction has exposed the reality that many times outstanding research efforts to define the burden of disease or the effectiveness of the vaccine have not led to local demand for the vaccine. It is now recognized that it is advocacy based on these data that has been missing from these efforts. Generating local advocacy from research requires that researchers include local opinion leaders in the process of designing research and surveillance projects and that the results of these efforts be dissemi-

nated through regional networks to key decision-makers and opinion leaders. In areas where Hib vaccine introduction has been quite successful (e.g. the Region of the Americas), a strong regional network exists that helps to achieve these objectives.

Activity: At the regional/sub-regional level, networks of key researchers, clinicians, and policy-makers should be formed to determine for themselves the key data that will be needed for introduction of pneumococcal conjugate vaccines in their region, and to develop a strategy for obtaining the data.

E. Evaluating vaccination regimens appropriate to the developing world

E.1 - E.3 Evaluating immunization strategies designed to protect very young infants

Rationale: Very young infants (<3 months old) suffer a disproportionately high burden of pneumonia mortality in many developing countries. The vaccination schedules evaluated in industrialized countries that give only one dose of vaccine before the age of three months are not well-suited to protecting these children. Infants <3 months of age might ultimately be protected by one of three approaches:

1) decreased transmission (e.g., herd immunity) generated by routine vaccination of older infants and siblings;

2) direct protection by schedules that give the first dose of pneumococcal conjugate in the neonatal period; and

3) passive protection by transfer of antibody from vaccinated mothers. Currently, there are limited data to evaluate the potential effectiveness of any of these approaches.

E.1 Evaluating the herd immunity effects of routine infant immunization on young infants (Priority level 2)

Activity: In ongoing trials and in early-introducing countries, evaluate the impact of routine immunization on the incidence of invasive pneumococcal disease in young infants (i.e., infants too young to be directly protected by vaccination).

E.2 Evaluating the safety and immunogenicity of neonatal immunization schedules (Priority level 2)

Activity: Conduct two to four studies of the safety and immunogenicity data of pneumococcal conjugate vaccine regimens that include a neonatal dose. Based on these data, determine what, if any, additional data are needed.

E.3 Evaluating the safety and immunogenicity of maternal immunization (Priority level 3)

Activity: Conduct additional phase 2 studies of safety and immunogenicity of maternal vaccination. Based on results from these studies and other approaches aimed at preventing early disease, it can be determined later whether additional studies, including phase 3 studies, are needed.

E.4 Evaluating the safety, immunogenicity, and efficacy of pneumococcal conjugate vaccination in HIV infected children (Priority level 3)

Rationale: HIV infection significantly increases the risk and severity of pneumococcal disease and may also adversely impact the safety and efficacy of vaccination. In some countries, the prevalence of HIV infection may be sufficiently substantial that countries may not consider introducing pneumococcal conjugate vaccines until the safety and immunogenicity has been established in this population. Data from studies conducted in industrialized countries where children routinely receive anti-retroviral therapy may not be considered sufficient to justify the use of the vaccine in populations where anti-retroviral therapy is not routinely used. A major phase 3 efficacy trial of pneumococcal conjugate vaccine currently underway in Soweto, South Africa, may provide an estimate of the vaccine's efficacy in HIV-positive infants.

Activity: The need for additional data should be re-evaluated when results from the ongoing trial of safety, immunogenicity, and protective efficacy among HIV-infected infants in South Africa is completed. Additional studies of the safety and immunogenicity of pneumococcal conjugate vaccination of HIV-infected children who are not on anti-retrovirals (i.e., populations typical of the developing world) may be needed.

E.5- E.6 Evaluating regimens of fewer doses of pneumococcal conjugate vaccination

Rationale: The four-dose regimens that have been evaluated in industrialized country efficacy studies are not the most appropriate for most developing countries. The most significant limitations of these regimens are their cost (25% > than 3-dose regimens) and the fact that they depend on a booster dose in the second year of life, a dose that is not widely administered in many developing countries. Ongoing efficacy trials in South Africa, the Gambia, and the Philippines are evaluating 3-dose regimens, but fewer dose regimens may also be attractive.

E.5 Evaluating 1 or 2-dose regimens of pneumococcal conjugate vaccination (Priority level 2)

Activity: Additional phase 2 safety/immunogenicity studies of 1 or 2-dose regimens are needed. These immunogenicity studies should include evaluation of immunologic memory and protection against nasopharyngeal colonization. If data demonstrating substantial safety immunogenicity and efficacy against carriage are promising, then studies designed to estimate protective efficacy of 1 or 2-dose regimens should be considered. The appropriate design (phase 3 or phase 4; controlled or uncontrolled) will need to be adapted to local conditions.

E.6 Evaluating mixed regimens of pneumococcal conjugate and polysaccharide vaccine (Priority level 3)

Activity: Consider conducting studies of the safety and immunogenicity of a prime-boost approach using conjugate vaccine followed by polysaccharide vaccine, with special attention paid to the issue of hyporesponsiveness following polysaccharide vaccine use.

F. Facilitating licensure of vaccines appropriate to developing countries and recommendations for their use

F.1 Develop standard materials and methods to license and release pneumococcal conjugate vaccines (Priority level 3)

Rationale: Regulatory authorities in industrialized countries may be reluctant to spend effort licensing vaccines that will not be used in their country (e.g., combinations that include diphtheria-tetanus-whole cell pertussis vaccines). On the other hand, these may be the vaccines that are most appropriate for and demanded by developing countries. Standardized methods for evaluating and testing vaccines will help accelerate the licensure process by assuring that all the data reviewed by regulatory authorities is of a high quality.

Activity: Develop and disseminate standard analysis methods and reference materials for: testing product for release; testing specimens for immunologic evaluation (e.g., standard ELISA); and characterizing products going into trials that are not being reviewed under an IND (or similar process) in the country of manufacture.

F.2 Establish and reinforce immunization practice advisory committees at the country level (Priority level 3)

Rationale: Eventually developing countries may be faced with the need to consider recommendations for using pneumococcal conjugate vaccines in ways that are appropriate to their local situation and priorities but are not supported by the strict label indication (i.e., off-label use). In many countries, there are standing committees or recommended bodies composed of experts in the areas of vaccination, child health, and immunology who are empowered to make these recommendations. In countries where these bodies do not exist or are not sufficiently strong, this may represent an obstacle to the process of taking a decision on pneumococcal vaccine introduction.

Activity: At a national, sub-regional, or regional level, develop and strengthen regional recommendation bodies that represent key professional societies in the country with expertise in vaccines, child health, epidemiology, immunology, and clinical research. These bodies could serve to review data on alternative regimens or products (e.g., combinations) and to issue recommendations for local use of vaccines.

Beyond infant pneumococcal conjugate vaccination

Though the focus of this meeting was on pneumococcal conjugate immunization of infants, the meeting participants recognized that there is a substantial burden of pneumococcal disease among adults and that comprehensive prevention of all pneumococcal disease may be enhanced by evaluating other approaches to pneumococcal vaccination (e.g., common protein vaccines). Further efforts to define the burden of pneumococcal disease among adults in developing countries and to evaluate the use of pneumococcal conjugate vaccines in this age group were encouraged. To accelerate the evaluation of candidate pneumococcal vaccines that may offer broad protection against all pneumococcal serotypes, the GAVI Task Force on Research and Development was urged to convene a meeting to determine ways to further the development of these alternative vaccines.

Summary of activities, by priority

Very important and urgently needed

A.1 Developing a range of methods to assess key disease-burden measures in different settings

A.2 Standardizing interpretation of chest x-ray pneumonia

B.1 Expanding surveillance for laboratory-confirmed pneumococcal disease

B.2 Measuring the burden of pneumonia

C.1 Continuing evaluation of the impact of immunization in efficacy populations and high-risk populations of industrialized countries

D.1 Generating more local advocacy and ownership from existing and future research efforts

Important but can begin in the next 12-18 months

B.3 Evaluating the key disease-burden outcomes in each region

B.4 Establishing the economic impact of pneumococcal disease and the potential cost-effectiveness of immunization

C.2 Establishing the efficacy/effectiveness of pneumococcal conjugate vaccination against key endpoints in developing countries

E.1 Evaluating the herd immunity effects of routine infant immunization on young infants

E.2 Evaluating the safety and immunogenicity of neonatal immunization schedules

E.5 Evaluating 1 or 2-dose regimens of pneumococcal conjugate vaccination

Important activities whose conduct is influenced by the results of antecedent activities

E.3 Evaluating the safety and immunogenicity of maternal immunization

E.4 Evaluating the safety, immunogenicity, and efficacy of pneumococcal conjugate vaccination in HIV-infected children

E.6 Evaluating mixed regimens of pneumococcal conjugate and polysaccharide vaccine

F.1 Developing standard materials and methods to license and release pneumococcal conjugate vaccines

F.2 Establishing and reinforcing immunization practices advisory committees at the country level

Annex 7.3
Fast-tracking rotavirus vaccine development and introduction in developing countries

Report of rotavirus meeting to prepare a global agenda, 14-15 May 2001, Geneva

Recommendations from meeting

Despite advances in the prevention and treatment of diarrhoeal diseases, rotavirus remains the principal cause of severe, dehydrating diarrhoea in young children worldwide. All children are infected with this virus and approximately 600,000 children die each year, or roughly 1 in 20 deaths among children less than 5 years old. Most of these deaths occur in poor, developing countries. Rotavirus vaccines have been promoted as the principal and best option for prevention of rotavirus-associated mortality and morbidity. The GAVI Task Force on Research and Development has selected rotavirus vaccines as one of three specific priorities to be targeted for accelerated development and introduction into developing countries within the next seven years. This choice was based on the high disease burden and the technical feasibility of making rotavirus vaccines. Rotavirus vaccines represent a "low-hanging fruit" for new vaccines because the principles for developing live, oral rotavirus vaccines have been well established, the manufacturing methods represent traditional cell culture, and the impact of a vaccine should be measurable within a year of introduction.

The summary and recommendations below represent the conclusions from a meeting held in Geneva on 14-15 May, 2001. The goals of the meeting were to identify priority activities that, if completed, should expedite the evaluation and introduction of rotavirus vaccines in immunization programmes in developing countries. To be consistent with GAVI objectives, these activities should be achievable within the next seven years. The recommendations are divided into categories that loosely correspond to the existing structure of GAVI task forces, although completion of many of the activities clearly will require input and expertise from many groups, within and outside GAVI. Comments on these recommendations will be solicited from a wide range of experts and the document will be made available for public comment.

1. Research and development

1.1 Principles of development and evaluation of candidate rotavirus vaccines for use in developing countries

- We anticipate that over the next five to seven years, multiple live, oral rotavirus vaccines will be developed by both multinational and local producers. This diversity of manufacturers will require partnerships between the public and the private sector and between local producers, outside experts and donor agencies. Given the need for a global supply of quality vaccine available at reasonable cost, and in the absence of information that one vaccine is substantially better than another, all producers capable of addressing these goals should be encouraged.

- GAVI should play a catalytic role in the development of safe and effective rotavirus vaccines that will be designed and intended for use primarily in the developing world.
- Research should focus on development of live, oral vaccines based on rotavirus strains derived from humans and animals.
- Clinical evaluation of vaccines should proceed in a step-wise fashion, with site preparation, phased clinical trials in representative populations and, finally, vaccine trials among special populations of infants.
- Primary efficacy endpoints for future trials should be severe rotavirus disease as measured by reduction in cases presenting to health system facilities (e.g., clinics or hospitals); efficacy against mortality should be estimated where possible.
- All clinical trials should be conducted in a scientifically rigorous manner.
- All clinical trials must incorporate adequate surveillance for intussusception to address local and global safety concerns but trials should not be unnecessarily delayed pending additional data on the pathogenesis of intussusception.
- Development and evaluation of rotavirus vaccines prepared by multinational vaccine manufacturers should proceed in parallel in developed and developing countries.
- Vaccine development and production by developing country manufacturers should be encouraged through technology transfer and/or collaboration with developed country partners.

1.2 Obstacles to vaccine development and evaluation

- The association between a rhesus-based rotavirus vaccine and intussusception observed in the United States may produce a variety of hurdles to overcome, including the need for large sample sizes in proposed trials to ensure an adequate level of safety.
- Lack of efficacy data from several regions of the world may delay uptake of vaccine in those regions.
- Some rotavirus vaccine candidates performed poorly when tested in developing countries. The reasons for this are not fully known, but may relate to poor trial design and execution.
- The variable epidemiology and strain distribution in developing countries may require alternative strategies compared to developed countries.
- Immune correlates of protection against rotavirus disease are as yet poorly defined. Clinical trials of adequate size will therefore be required to establish the efficacy of each new candidate.
- Data on safety and efficacy of vaccines in special populations, such as HIV-infected, malnourished or premature infants, will be required t0 make global recommendations.

1.3 Priority activities

The development and testing of a variety of candidate rotavirus vaccines for use in developing countries will require creation of a variety of partnerships related to the companies that develop the vaccines.

a) Field trials to evaluate the safety and efficacy of candidate live, oral vaccines produced by multinational manufacturers should be conducted in developing countries.

   Testing of rotavirus vaccines should be conducted concurrently in developed and developing countries to assess differences in vaccine behavior that might reflect differences in the epidemiology and strain distribution of rotavirus infections Parallel testing in developed and developing countries might encourage the manufacturers to consider and plan for global supply.

   Since developing countries are not a primary target for multinational companies, some international financial and technical resources should be made available to encourage and support these clinical trials in developing countries and to ensure that the efficacy of these vaccines is clearly demonstrated among children in developing countries. Such studies might lead to alterations in the vaccine dose, schedules, formulation or acceptability that would speed subsequent introductions.

b) The GAVI partners should be encouraged to provide financial and technical resources to support developing country clinical trials of vaccines produced by developed country manufacturers.

   Manufacturers that currently produce oral poliovirus vaccines using cell culture technology have the capability to produce live, orally administered rotavirus vaccines if technical support is available. Partnerships between developing country manufacturers and scientists from developed countries could serve as a model for technology transfer and local production of vaccines.

c) A well-designed, randomized, blinded, controlled field trial should be conducted with the Lanzhou Lamb Strain (LLR) vaccine to establish safety and efficacy.

   (i) Review the production methods of the LLR vaccine and obtain consultation and technical support to assure that it adheres to acceptable standards of quality.

   (ii) Should other candidate vaccines be produced in China, they should be rigorously evaluated for efficacy in the same manner.

d) A standard protocol including standard case definitions and treatment protocols should be developed for use in field trials to ensure sensitive detection and optimal treatment of intussusception cases that occur among infants enrolled in clinical trials,

e) Clinical trials of all vaccines should provide sufficient data on intussusception for decision-making for local, regional and global use. Risk-benefit analyses should be conducted for developing countries incorporating data on safety (including intussusception risk, if any) and local data on disease burden and other factors.

f) Encourage and continue studies to better define immune correlates of protection from rotavirus disease by ensuring that all trials include methods to assess markers of immune response.

g) Ensure data on safety and efficacy are collected among special populations, such as infants with HIV infections, premature infants, and infants with ongoing diarrhoea.

2. Ensuring availability of a rotavirus vaccine

2.1 Principles for ensuring adequate supply, forecasting demand and assuring quality of vaccines for use in developing countries

- Process for ensuring vaccine availability should be a joint activity shared between the public sector and industry partners.
- These activities involve essential links to other GAVI partner activities.
- Discussion regarding the activities below should begin early, even for those where necessary data are not yet available, so as not to delay vaccine introduction.

2.2 Obstacles to ensuring vaccine availability

- Some estimates used to determine demand will not be known until vaccines are closer to introduction.
- Others?

2.3 Priority activities

a) The GAVI Forecasting Group and the GAVI Financing Task Force should be responsible for developing reliable estimates of demand for rotavirus vaccines

(i) Identify which countries will use rotavirus vaccines and develop country-specific estimates. Priority should be given to the 16 countries that vaccinate more than one million children annually.

(ii) Assuming that rotavirus vaccine will be administered in a routine EPI programme, calculate the actual number of children to be immunized by using the product of coverage rates and the birth cohort of the countries.

(iii) Financing commitments and options should be clarified. This will require a clear statement of intent from GAVI and the Boards of GAVI and The Vaccine Fund.

(iv) Develop estimates of timeframe for vaccine introduction and uptake of vaccines.

b) Work with manufacturers to determine the incremental costs of scaling up production to ensure sufficient quantity of vaccine for developing countries.

c) Consider sharing with manufacturers the costs of conducting parallel vaccine trials in developing countries.

d) Work with manufacturers to limit their risks in producing rotavirus vaccines, including:

(i) Providing the best demand forecasts, so that scaling-up time is allowed for and so that capacity for producing doses of vaccine for developing countries is planned.

(ii) Discuss price indexing for different markets.

(iii) Consider options to limit liability related to intussusception, both financial and the reputation of the company. This may include advocating for liability insurance for adverse events.

e) Discuss funding mechanisms that would promote use of rotavirus vaccines in developing countries, such as tiered pricing.

f) Work with the Developing-Country Vaccine Manufacturing Network to address issues specific to developing countries.

g) Clarify GAVI's role in supporting developing-country manufacturers.

h) Ensure that vaccines produced in developing countries meet internationally acceptable standards of quality, safety, efficacy, and consistency.

(i) Determine who will provide regulatory oversight:

- Begin dialogue with FDA and the European medical regulatory body (EMEA).
- Strengthen national regulatory authorities (NRAs).
- Target NRAs of likely production and trial countries to develop expertise related to rotavirus.
- Convene national and regional expert panels (and increase expertise of panels) for off-label use and recommendations.

(ii) Ensure that the clinical programme for vaccine development ensures adequate safety and efficacy assessment to provide global approval:

- Ensure scientific support to ensure questions related to intussusception are adequately addresses taking in to account national and regional considerations.
- NRA's in countries where trials are planned should be educated regarding issues of intussusception surveillance.
- Ensure that rotavirus vaccine development promotes internationalisation of results
- Engage in consensus building on scientific issues, such as cell substrates.
- Develop international guidelines and recommendations on production and quality control.
- Develop appropriate international standards and reference reagents.

3. Disease burden of rotavirus and advocacy for rotavirus vaccines

3.1 Principles for developing advocacy of rotavirus vaccines for use in developing countries

- Currently, inadequate awareness of rotavirus disease burden exists among all levels of society.
- Reliable estimates of disease burden will be helpful in advocating the need for rotavirus vaccines.
- The need for an effective rotavirus vaccine exists worldwide, although the targets of the vaccine may be different in different settings; this will affect advocacy of vaccine.

3.2 Obstacles to advocacy of rotavirus vaccines

- In many regions and countries, data on rotavirus disease burden are either limited or outdated.
- Diagnostic capabilities to rotavirus are lacking in many places where the disease burden may be highest.
- Since diagnosis of rotavirus is perceived to add little to clinical practice, inclusion of rotavirus diagnostics in many places will be difficult.
- The association between a rotavirus vaccine and intussusception will require significant efforts to overcome.
- No vaccine is currently available; this makes advocacy efforts more difficult.
- Few decision-makers are aware of rotavirus.
- Since vaccines against rotavirus will prevent a fraction of all diarrhoeal events, developing a clear message will be essential.

3.3 Priority activities

a) Complete the creation of a simple, generic protocol for estimating the rotavirus disease burden in developing countries.

b) Implement studies based on the generic protocol in countries that are expected to consider the use of rotavirus vaccines.

c) Establish regional networks for surveillance and estimation of the disease burden for rotavirus.

The networks are encouraged because they provide an opportunity to share regional expertise and costs of surveillance, offer foundations for training and infrastructure building, produce standardized, comparable data, and offer efficient mechanisms to collect reliable data for local decision-making. The studies should be based on hospital-based surveillance, as described in the generic protocol and include a strong-strain surveillance component. Involvement of local and regional experts and public health officials should be encouraged. Each participating

country should develop methods for evaluating local health care utilization practices with respect to diarrhoeal diseases; this will facilitate comparison of data between countries.

d) Conduct three larger, more involved, diagnostic demonstration projects, in the Region of the Americas, the African Region and in Asia.

Objectives of the studies will be to clarify disease burden at multiple levels of severity (e.g. hospitalizations, clinic visits, community illness) to refine methods for monitoring the impact of vaccine, to survey and follow trends in knowledge, attitudes and practices related to rotavirus disease and vaccine, and to define costs of disease in specific settings.

e) Conduct a thorough review of existing literature and model mortality data to derive updated global and country-specific estimates.

f) Consider conducting probe studies in the setting of vaccine effectiveness studies in areas of expected high diarrhoeal mortality.

It will be important to work with manufacturers and trial sites early to ensure that appropriate methods are included in study protocols.

g) Develop methods to estimate mortality burden attributable to rotavirus at the country level.

h) Develop standard methods to estimate incidence and epidemiology of intussusception in developing countries. Conduct studies in settings where trials will be conducted or where early introduction of vaccine is considered.

i) Work closely with advocacy experts on rotavirus-specific issues, such as clarifying intended messages with respect to the risk of intussusception and the real and perceived efficacy of vaccines, and increasing the awareness of rotavirus disease among practitioners and communities (i.e., put a “face” on the disease).

j) Support the creation of champions at many levels, including international agencies and organizations, regional groups, medical societies, ministries of health and others.

k) Conduct surveys to determine knowledge, attitudes and practices concerning rotavirus among decision-makers, clinicians and communities.

l) GAVI should adopt, promote and up-date in a timely manner a seven-year research agenda to expedite rotavirus vaccine introduction into developing countries.

m) GAVI should serve to facilitate consensus-building regarding the research agenda, and may develop mechanisms to coordinate the priority activities.

n) Partners should begin efforts to ensure programme feasibility of rotavirus vaccines, including the creation of recommendations regarding vaccine formulation and presentation, in order to expedite incorporation into existing expanded programmes on immunization (EPIs).

Annex 7.4
Report on proceedings of the GAVI Workshop on new technologies

NIH, Bethesda, Washington, 17-18 April 2001

Purpose of the workshop

A group of experts in new technologies were brought together with representatives with field experience of immunization issues to exchange knowledge and reach a decision on how to progress with strategies to improve the safety, access, utilization, effectiveness, utility or performance of immunization in developing countries.

The objective of the workshop was to:

1) Exchange knowledge of what is happening in the field and the possible technologies/research we could be considering.

2) Agree the priority strategic goals we should be addressing – i.e., the priority strategic issues, the most critical needs of the developing countries for new technologies or research in the short and long term.

3) Identify a preferred set of strategic options we could pursue to address these issues, narrowing the options to a manageable set.

4) Discuss and agree a set of criteria that could be used to evaluate which technologies or research we should be developing as priority.

It was anticipated we would emerge with three priority technology or research areas we would take forward for further evaluation.

These objectives were only partially met, as there was a reluctance by some of the GAVI participants to reduce the options at this stage.

Agenda

The meeting agenda included a series of excellent presentations by field representatives and experts on new technologies, given over the first day and a half of the workshop. The last afternoon was devoted to discussion of the strategic issues we should address and how to proceed.

- Mike Levine and Teresa Aguado set the scene with a description of GAVI's role and operation, particularly the role of the Task Force on R&D. They also set the scene for the expectations of the outcome of this workshop.

- Mark Kane spoke on how the Task Force on R&D relates to other GAVI task forces in achieving GAVI's objectives. He spoke of the GAVI objective to improve immunization in developing countries by investing in vaccines, technology and capacity building. In relation to new technologies, he spoke of improving:

- Coverage from 60% to 80%
- Wastage from 60% to 10%
- Safe vaccination from 60% to 100%. In this respect it was noted that immunization injections constitute only about 10% of all injections, and that these are generally the safest injections given. Safety can be addressed through both administration and technology.

He also spoke of the need for a new delivery platform technologies which would enhance the ability to meet immunization goals in developing countries and suggested that, by coordinating efforts and focusing towards a tangible goal (e.g. a particular disease), we could more effectively utilise the new technologies to improve immunization services.

- Peter Wilson, the facilitator, explained the process for the workshop and presented feedback of the results of the questionnaire which had been distributed to some 65 experts and representatives among the GAVI partners worldwide, over a third of whom were in developing countries. The results of the questionnaire are outlined separately below. There were 41 responses, 12 of which were from developing countries.
- Dr Rudolph Cummings from Guyana outlined some of the immunization issues experienced in his country. These included:
  - Variations in the quality of the ten different health regions; immunization in the interior is less efficient.
  - Transport costs and local transport issues, wastage rates (population density and multiple-dose vials), migrant population and lack of trained staff were some of the key issues.
  - The problems they experienced with solar power were particularly informative, as now more than half of the solar-powered appliances installed just a few years ago are not working. New technology is fine, but there needs to be sufficient trained staff to maintain the technology, as well as an infrastructure to support it.
  - Experience with auto-disable syringes had not been good.
- The second scheduled speaker from a developing country was unable to attend.
- Michael Free gave a comprehensive description of PATH's initiatives in new and appropriate technologies in support of immunization. PATH's focus for Technology is on:
  - Safe and effective vaccines at the point of administration:
    No heat damage
    No freezing damage
    No contamination
  - Safe administration:
    Assuring sterile injections
    Self-contained unit-dose delivery systems (SCUDDS)
    Preventing sharps injury

- Vaccine accessibility:
  Adequate and timely delivery of supply
  Assured availability of means of administration
  Adequate storage capacity
  Adequate outreach capacity

- System efficiency:
  Fewer administrations
  Reduced dependency on the cold chain
  No vaccine wastage
  Just-in-time logistics
  Minimum equipment down-time

He also presented a detailed system for evaluating technologies.

- Gene Tutwiler presented Universal Preservation Technologies Vitrolife process for glass state, which could be used to make vaccines stable at room temperature and reduce dependency on the cold chain. Positive results have been achieved with the technology, but further development work is required for vaccine application, notably in scale-up development, aseptic technology development, immunogenicty studies and delivery using non-aqueous systems.

- Bruce Weniger outlined the work being done at the US Centers for Disease Control and Prevention (CDC) on needle-free immunization. Short-term solutions include the use of disposable cartridge jet injectors, with a need for universal cartridges. Many jet guns are now in development. Longer-term alternatives include inhalers, sugars and nucleic acid. If this route is to be taken, there is a need for a generic injector with a standard cartridge fitting, which implies a meeting of partners to agree on a standard. Commercial production could start soon thereafter.

- The Becton Dickinson representative gave an outline of some of the new technologies being developed for needle-free delivery. These include:

  - Mucosal flu vaccine delivery already being used in the market. Accuspray is a novel nasal vaccine-delivery system which one can even use for self-administration.

  - Silicon microchip swipe for skin-based delivery direct to Langerhans cells

  - OnVax – some antibody delivery based on subunit delivery including DNA and CTL in small animal models

- Robert Steinglass of BASICS spoke of key issues in immunization services and how improved systems and operational research could address some of these issues. Coverage of immunization stagnated during the 90s and, in some cases, dropped off – understanding why this has happened is very important. It is also important is to have reliable data on which to make the assessment of immunization effectiveness and coverage. There are limits to technological solutions in the field (as demonstrated by the solar power problem in Guyana), and a need for better feedback systems of problems that arise. Both appropriate technology and the better utilisation and simplification of existing technology are required. A step-wise approach to improving immunization services should be adopted – first improve access, then raise demand, then improve performance and, finally, improve the

quality of service. System strengthening should be combined with active monitoring, decentralized advocacy and community involvement.

- Neil Constantine presented an array of diagnostic methodologies for detecting antibodies and antigens, indicating that this technology is improving rapidly in sophistication. Indications are that the tests will be procedurally simple, stable and robust at different temperatures, portable, and with configurations which allow for multiple analytes. Apart from finger-prick blood tests and urinary tests, oral fluid (saliva) testing is also being developed. Results from these tests can be available within minutes.

- Mike Levine spoke of the developing opportunities in mucosal delivery, and particularly oral, to simplify immunization processes and potentially increase coverage. Research into adjuvants and antigen delivery systems is having some success in enhancing the immunogenicity of mucosal and oral delivery. There have, however, been some disconcerting observations with mucosal vaccines, and a loss of immunogenicity when moving vaccines from the developed world to developing countries.

- Charles Arntzen gave a detailed account of the work his team have been undertaking with edible vaccine technology. Some interesting results have been achieved, and the technology holds promise. However, trials for vaccine applications are at an early stage.

- Reinhard Gluck and Gordon Dougan spoke on advances in vaccine technology that would allow for fewer patient contacts for the same immunization coverage. This covered the field of adjuvants, antigen delivery systems, and multi-valent vaccines. Much research is going on in all these fields, particularly in industry, as these have both developed world and developing world applications. Reinhard Gluck spoke in detail of the successful launch of their intranasal flu vaccine, and the technological developments it captures.

- Gregory Glenn of IOMAI outlined the work they have been doing on transcutaneous patches for delivery to the Langerhans cells. Hydration techniques have considerably improved response, as have the use of adjuvants. Early results for delivery of vaccines have been encouraging, but trials are in early stage. Five trials have been performed with four planned for the future.

- William Egan cautioned the group on the requirement for regulatory approval for all these new technologies. Vaccines are licensed for a particular delivery regime – if the delivery is changed (e.g. from syringe to jet gun), or the vaccine is delivered in combination, for example, the immune response could change, or there could be some adverse response profile. Adjuvants, for example, are not licensed – they are only licensed in combination with specific antigens. Thus each change would need to pass regulatory approval.

- Alan Shaw also cautioned on the practical and commercial implications of taking up new technologies or new approaches. Taking the example of MMR, he explained how a sugar/glass formulation of MMR could take at least five years to license when you go through the complex procedures of processing and testing, product development, clinical trials, regulatory approvals, etc. During this time there are other projects competing for the resources which could well achieve greater

commercial returns. It could be suggested that one utilises these new technologies with new vaccines but, again, one does not want to complicate the uncertainties in the development process. One already has a major risk in the performance of the new vaccine, and hence one wants to reduce the risk by keeping other variables as safe and known as possible. One could take the burden off industry by offering to do trials for them, but industry is reluctant to do this, as an improperly administered trial with adverse results could have disastrous consequences for the company's own product.

Results of the questionnaire

The 41 responses were analysed in three categories:

- Developing countries (12 respondents)
- Specialists (four responses from PATH and CDC)
- Others from developed countries

Analysis of the responses indicated that:

1) In terms of the role (or goal) of new technology or research, there were some interesting outcomes:

   - The most important role for new technologies was seen to be the need to make immunization simpler, easier, and more practical.
     - Developing countries saw this as the most important goal.
   - The second most important role was to increase access, coverage and utilization (i.e., combining the two access responses, since respondents considered them to be similar).
     - Developing countries saw this as the second most important goal.
   - The third most important role was considered to be to make immunization safer.
     - The specialists rated this highest, while developing countries rated it second lowest.

2) For the criteria to be used to select the new technologies:

   - The most important, by far, was considered to be the potential impact of immunization on safety, access, performance, etc.
     - Increasing immunization coverage was seen to be the most important measurement of impact.
     - However, the combined scores for measurement of mortality and morbidity pointed to it as the most important measurement of impact.

- The next most important criteria in close descending order were:

  - the probability of technical success in a short/medium timeframe.
  - programme feasibility.
  - sustainability of the application of the new technologies in developing countries.

3) In assessing which technology or research areas were likely to have the greatest impact, and should hence be supported, there were some interesting variations in responses from the different groups:

- The developing countries gave greatest support, in descending order to:

  - technologies which will reduce the number of patient interactions (contacts);
  - reducing dependency on the cold chain and temperature stability;
  - field and operations research.

- The specialists gave greatest support to:

  - elimination of non-sterile injections;
  - unit-dose delivery

- Overall, greatest support, in descending order, was for:

  - elimination of non-sterile injections, unit-dose delivery and prevention of contamination (when all combined);

  - reducing dependency on the cold chain and temperature stability;

  - technologies which reduce the number of patient interactions.

4) When it came to ranking more specific technologies, there were distinct differences in the short term and the longer term. For short term action, the technologies or research which were rated highest by all respondents were, in descending order:

- improved management and tracking systems in the field;
- temperature-stability technologies;
- operations and field research;
- multi-valent and multi-vaccine administration.

In addition:

  - developing countries gave high rating to “engineering solutions” (i.e., appropriate technologies to solve engineering problems, such as cold chain);

  - the specialists rated Uniject, pre-fill technologies and Monodose highly, together with waste handling.

5) The longer-term technology solutions showed a clear lead for the highest ranked technology area:

- non-parenteral delivery was rated almost twice as highly as any other generic technology area (e.g., transcutaneous, oral, mucosal, etc);

- reducing dependency on the cold chain and temperature stability was clearly second;
- third was multi-valent and multi-vaccine delivery;
- fourth was needle-free parenteral delivery.

The questionnaire results showed some clear trends:

1) The desire to make immunization simpler and easier, by:
   - reducing the number of patient interactions
   - improving management and tracking systems
   - solving the short-term engineering problems (e.g. cold chain).
2) Reducing the dependency on the cold chain, which appears to be a major source of difficulty.
3) Reducing the use of sharps in the long term and moving to non-parenteral immunization.
4) Seeking ways to make immunization safer.
5) The need for a better understanding of the effectiveness of immunization services and factors affecting immunization access and coverage, so that these can be improved.

The way ahead

A debate on the way ahead brought out two different schools of thought:

1) One school of thought favoured identifying some higher-level goals, then building a tree of technologies that could be evaluated to best achieve those goals. Three goals were identified:
   - safety
   - programme effectiveness
   - system efficiency
2) The other school of thought argued that a limited set of key technology or research issues had already been identified through the questionnaire and the views of the participants at the workshop, and that we should rather debate and rank which of those issues we should evaluate in more detail, bearing in mind that we have both short- and long-term goals. A preliminary list of these issues were:
   - reducing dependency on the cold chain
   - reducing the use of sharps
   - reducing the number of patient interactions
   - expanding access
   - safety
   - data for decision-making

After much discussion, it was decided to go with the former approach (1 above) as it was considered too soon to be narrowing down to specific technology areas; group of experts should be co-opted into teams to evaluate the technologies which would best achieve the goals set our under 1) above.

Provisional trees for each of the three issue areas were drawn up.

Safety

1) heat safety:
   - sold chain management
   - vaccine vial monitors (VVMs)

2) freezing damage

3) contamination

4) preventing re-use:
   - monodose
   - Uniject
   - SCUDDS
   - auto-disable syringes

   auto-reconstitution

5) preventing sharps injuries

6) safe disposal

7) proper techniques

   In the longer term: needle-free SCUDDS
   - non-parenteral
   - safe jet injectors

Programme effectiveness (access, availability, utilisation)

1) Access
   - outreach capacity
   - reaching the unreached: expanding the age groups
   - reduce drop-outs
   - storage

2) Reduce number of contacts
   - multi-valents

3) Programme management
   - systems
   - logistics
   - management information systems

4) Monitoring and surveillance

field and operations research
surveys
serosurveys
outcomes assessment

5) Improve existing cold chain

In the longer term: Outsource

System efficiency

1) Reduce dependency on the cold chain
   - glass technologies, etc
   - thermal stability

2) Reduce number of contacts
   - multi-valents
   - multi vaccine administration

3) Reduce wastage
   - monodose, etc.
   - better vaccines

4) Efficient management
   - information technology (IT) systems
   - transport
   - logistics systems

5) Easier processes
   - longer term:
   - non-parenteral immunization
   - SCUDDS
   - cold chain
   - multi-valents
   - vaccine vial monitors (VVMs)
   - auto-reconstitution
   - etc.

Criteria

The following criteria were suggested by the task force, and should be taken into account by the evaluation teams when assessing the technologies to be supported in going forward.

1) Impact, to be defined by:
   - contribution towards meeting the stated goal (e.g. administration safety);
   - the amount of input required to achieve the impact (minimum).

2) Programme feasibility and sustainability.

3) Technical and production feasibility.

4) Does it make immunization simpler, easier and more practical?

5) Cost of adoption versus benefit.

6) Catalytic – not being done elsewhere, and could lead to further benefits.

The teams would be encouraged to "think big, and to think long term". Between the teams, however, there would need to be some short-term solutions, and some longer-term thinking.

Study teams

It was recommended that up to three study teams be set up to research and evaluate a strategy to achieve the immunization goals set out above, namely:

- Administration safety
- Programme effectiveness
- System efficiency

A different team will study each goal.

The teams will be required to:

- better define the strategic goal (given) that they will be trying to achieve in immunization in developing countries;
- identify the main issues and constraints in achieving that goal;
- develop preferred strategies to address these issues and constraints, such as:
  - possible technologies or research,
  - both short term and long term;
- evaluate a short list of preferred strategies against the eriteria;
- recommend preferred strategies to meet the goal:
  - both short term, and long term.

Each of the teams should consist of equal numbers of new technology or immunization experts and developing country representatives. It is suggested each team should not consist of more than six people.

Next steps

- Agreement of the Task Force and the Working Group that this is indeed the way to proceed.

- If this is agreed:
  - Present the plan at the Montreux meeting. This will require:
    - more information on what each of the issue areas really covers, and a better definition of requirements in the study phase;
    - selection of a champion on each issue area to make a presentation at Montreux (e.g. Michael Free on administration safety).
  - Present the plan to the Board.
  - Appoint team leaders.
  - Invite people to sit on the teams.
  - Draw up terms of reference for the teams.
  - Agree report-back and interim requirements.

Annex 7.5
Briefing notes for the meeting on selection of vaccination technologies

17-18 April 2001, Bethesda, MD, USA

Meeting objectives

- Exchange knowledge of what is happening in the field and the possible technologies/research we could be considering;
- Agree on priority strategic issues, i.e. the most critical needs of the developing countries for new technologies or research in the short and long term;
- Identify a preferred set of strategic options we could pursue to address these issues, narrowing the options to a manageable set;
- Discuss and agree a set of criteria that could be used to evaluate which technologies and/or research areas we should be developing as priority.

Outcomes

1) The questionnaire results show some clear trends

- The desire to make immunization simpler and easier. That is:

  (a) reducing the number of patient interactions,
  (b) improving management and tracking systems, and
  (c) solving the short-term engineering problems (e.g. cold chain).

- Reducing the dependency on the cold chain, which appears to be a major source of difficulty.
- Reducing the use of sharps in the long term and moving to non-parenteral immunization.
- Seeking ways to make immunization safer.
- A need to better understand the effectiveness of the immunization service and factors affecting immunization access and coverage, so that these can be improved

In general, the results appear to indicate that safety considerations are more a concern to developed than to developing countries.

2) Selection of technologies

A debate on the way ahead brought out two different schools of thought:

One school of thought that favoured identifying some higher-level goals and then building a tree of technologies which could be evaluated to best achieve that goal. Three immunization goals were identified:

- Administration safety
- Programme effectiveness
- System efficiency

The second school of thought argued that a limited set of key technology or research issues had already been identified through the questionnaire as well as the views of the Task Force and invited experts at the workshop. We should now debate and rank which of these issues to evaluate in more detail, bearing in mind that we have both short- and long-term goals.

After much discussion, it was decided to go with the approach of the first school of thought (above), as it was considered too soon to be narrowing down to specific technology areas; a group of experts should be co-opted into teams to evaluate the technologies which would best achieve the goals above.

3) Criteria

The following criteria suggested by the Task Force should be taken into account when assessing the technologies to be supported in going forward.

- Impact, defined by:
  - contribution towards achieving the immunization goals;
  - the amount of input required.
- Programme feasibility and sustainability.
- Technical and production feasibility.
- Does it make immunization simpler, easier and more practical?
- Cost of adoption versus benefit.
- Catalytic – not being done elsewhere, and could lead to further benefits.

4) Study teams

It was recommended that up to three study teams be set up to research and evaluate a strategy to achieve the immunization goals set out above. The teams, which will function in a lean and efficient manner, will include members of the R&D Task Force, the TF on Country Coordination and appropriate *ad hoc* members who have the desired expertise. The teams will be required to:

- better define the strategies to achieve the immunization goals in developing countries;
- identify the main issues and constraints in achieving these goals;

- select possible technologies and/or research areas;
- evaluate a short list of preferred strategies against the criteria;
- recommend preferred strategies to meet the goal for:
  - the short term (achievable within five years), and
  - the long term (achievable within ten years).

The teams will consist of equal numbers of "new technology" or "immunization" experts and developing country representatives. It is suggested the teams should not consist of more than six people.

Next steps

- Agreement of the R&D Task Force and Working Group that this is indeed the way we wish to proceed.
- If this is agreed:

  10-12 June 2001:

  - Present the plan to the Montreux meeting:
    Ask a champion for each of the immunization goals to make a presentation
    Flesh out what each of the immunization goals really covers

  21-22 June 2001

  - Present the plan to the Board
  - Appoint study team leaders

  21-22 June through to early July 2001

  - Invite team members
  - Draw up terms of reference for the teams
  - Agree on mechanisms for inter-team co-ordination

  Oct/Nov 2001

  - Report back to GAVI Board meeting

Figure 1: Technologies to improve vaccination in low-income countries

Safety of administration	Programme effectiveness	System efficiency
GOALS		
• Avoid unsterile re-use • Reduce sharps	**Access/accessibility** • Reach the "unreached" • Expand targets • Reduce drop-outs	**Thermal stability** • Heat resistant • Freeze resistant • Reduce number of contacts (doses) • Reduce wastage (better vaccines)
STRATEGIES		
	Management • Information systems • Monitoring/assessment • Logistics/transport • Reduce wastage • Improved cold chain **Outcome assessment:** • Monitoring and surveillance	
TOOLS		
• Safe or pre-filled jet injection • Self-contained unit dose delivery system (SCUDDS) • Auto-disabled tools • Reconstitution • Improve waste disposal	• Pre-filled packaging; • Monodoses; • SCUDDS (Uniject, Imule); • Vaccine vial monitors (VVMs); • Auto-reconsitution; • Other technologies.	• Sugar-dried products; • Controlled release; • Oral vaccines; • Transdermal vaccines.

Annex 7.6
The meningitis vaccine project

For more than a hundred years, devastating epidemics of meningococcal disease have caused enormous suffering in the Sub-Saharan African meningitis belt countries. The belt stretches from Ethiopia in the east, to Senegal and the Gambia in the west, with a population of over 200 million at risk. Countries within the meningitis belt suffer from recurrent meningococcal epidemics, often in irregular cycles every 5-12 years. During an epidemic, attack rates are high in infants but also continue through young adults in the prime of life. The impact extends beyond the individual, becoming social and economic disasters for the countries affected. Due to their scope and immediacy, the required public health interventions are disruptive to other programmes and expensive; furthermore, they are only partially effective.

In order to prevent and ultimately eliminate epidemic meningococcal disease in the African meningitis belt, The World Health Organization (WHO) and the Bill and Melinda Gates Children's Vaccine Program at PATH (CVP) formed a partnership, in collaboration with the US. Centers for Disease Control and Prevention, to develop, evaluate and introduce serogroup A plus C meningococcal conjugate vaccines in Africa. The technology to produce a safe and effective meningococcal conjugate vaccine for Africa has been available for more than 10 years. Successful prototypes previously evaluated in African infants were immunogenic, and others for meningococcal C disease have already demonstrated impact in the United Kingdom. Yet, the meningococcal A projects were halted because serogroup A meningococcal disease is limited to persons in the poorest countries, and the returns on investment are perceived to be too low. The major obstacles identified by vaccine companies include the high cost of increasing conjugate vaccine capacity and vaccine development, and the high "opportunity" costs of failing to pursue projects that have a higher potential for return on investment.

The need for a better vaccine to prevent epidemics is well recognized at local, national and regional levels in Africa. Governments in the region perceive meningococcal disease as a major public health problem. Over the past four years, the African community has made clear its commitment to using a safe and immunogenic vaccine. On 5-7 April 2000, delegates from Burkina Faso, Ethiopia, Mali, Niger, Nigeria, Saudi Arabia, Sudan, and the Regional Offices for Africa (AFRO) and the Eastern Mediterranean (EMRO) gathered at the World Health Organization in Geneva to evaluate a variety of proposed strategies leading to the development of a meningococcal conjugate vaccine. Together with multilateral organizations, vaccine companies and the scientific community, their conclusions affirmed the goals of this project.

The project has been launched with core funding from the Bill and Melinda Gates Foundation, which awarded the partnership US$ 70 million over the next decade to:

- Develop a meningococcal A/C conjugate vaccine and evaluate it in Africa.
- Create a pathway for the licensure of vaccine which will be used largely in Africa.
- Assure production in sufficient volume to meet projected needs.
- Monitor the intervention throughout to assure its effectiveness and safety.
- Finance the procurement of vaccine through existing or global programmes.
- Introduce the vaccine through mass and routine immunization, in synergy with other public health programmes.

The meningitis vaccine project (MVP) will accomplish these goals in partnerships with vaccine companies whose proposals have already undergone extensive technical review. Further negotiation, development of realistic milestones and timelines are ongoing. The project will be presented after analysis to the Financing Task Force "Out-of-the-Box" group at the end of July 2001.

The GAVI R&D Task Force will hold a meeting in October 2000 in Africa to analyse in detail the R&D activities needed to achieve the goals of the Meningitis Vaccine Project and to review other approaches that are critical to advance the prevention of meningococcal meningitis in other areas.

Annex 8
Technology transfer: a strategy for vaccine supply

GAVI position statement

Technology transfer must not be treated as an end in itself, but should be considered as a means towards GAVI's larger objectives to accelerate the development of priority vaccines and expand the use of all vaccines.

Vaccine manufacturers from both industrial and developing countries are playing a critical role in meeting immunization needs. Technology transfer, joint ventures and direct investment are ways to encourage their expanded involvement in meeting GAVI objectives.

Over the last 15 years, regulation, science, technology, prices and public demand have all changed significantly. Ensuring that a manufacturer can develop, produce, license and sell a vaccine remains a complex process, involving building capacity in a number of areas covering not only technical expertise, but also regulation, new forms of partnership and accountability to consumers and civil society.

Globalization should imply not only the removal of trade barriers, but also the development of the appropriate frameworks within which innovation, competition and access by the poor to the benefits of new technology can thrive. Such frameworks include the development of new knowledge networks, accountability to consumers and civil society, global agreements on standards and quality, associated regulatory systems and the appropriate development of technical capacity and technology.

- Independent national regulatory authorities (NRAs) have been essential in driving quality and protecting consumers. Considering that approximately one-half of vaccine-producing countries have NRAs that achieve the six required regulatory functions as outlined by WHO[1] it is essential to develop and monitor this capacity.

- New vaccine technologies, such as conjugation, require different equipment, processes, know-how and testing procedures than those used to produce the traditional vaccines. As production costs for these new technologies are higher, increased access to the technologies depends less on where production is based but rather on reliable supply and best prices, whilst maintaining the quality demanded by governments and consumers.

- Experience has shown that successful technology transfer depends on a true partnership existing between the transferor and the transferee. This partnership, whether it is industrial-developing, developing-developing, or industrial-industrial, needs to be ongoing, mutually beneficial, and dynamic.

[1] See [http://www.who.int/vaccines-access/Vaccines/Vaccine_Quality/Strengthening_national_Regulatory/nra_six_control_functions.htm].

- One of the most important evolutions has been a change in the products demanded by developing and industrialized countries, as well as a change in suppliers of these products. This evolving market-place is creating new niches for manufacturers wishing to expand their presence in the developing world.

GAVI has identified meningococcal A/C conjugate, pneumococcal conjugate and rotavirus vaccines as priorities for accelerated development, scale-up and introduction. In addition, priority vaccine delivery technologies are being identified for development. Teams for each product are identifying the current obstacles and the most appropriate strategies and activities to address them. The role of technology transfer is being considered within these comprehensive work plans.

Continued investment in research and development is essential, both to push the frontiers of science and to translate scientific knowledge into useable products. GAVI needs manufacturers who will invest both capital and human expertise in the research and development of products that meet the needs of developing countries. While technology transfer may play a role in increasing production capacity of vaccines, it will not ensure investment in R&D of future vaccines. To meet current and future goals, GAVI must promote a fair and competitive market-place that harnesses all suppliers.

Annex 9
The development of guidelines on financial sustainability for countries

Status report

In June 2000, the GAVI Board charged the Financing Task Force (FTF) to develop guidelines for Vaccine Fund-eligible countries as to how improved immunization programmes can be sustained once catalytic support from The Vaccine Fund ends. The challenge is significant and growing, particularly given the commitment of GAVI, countries and their partners to move beyond maintaining today's immunization programmes. GAVI partners must plan now to sustain the improved immunization programmes of tomorrow.

There is an emerging consensus that, while responsibility for immunization rests fundamentally with the national government, for many of the lowest-income countries the sustainability of improved immunization programmes will be the shared responsibility of countries and partners for some time to come.

Efforts to date

Using a wide consultative process involving hundreds of individuals and organizations in both developing and developed countries, the GAVI Financing Task Force (FTF) has:

- established a 20-member FTF Financial Sustainability Group comprised of international health and financing experts to support the core FTF;
- commissioned Dr Ruth Levine et al. at the World Bank to write *Sustaining Immunization Programs: Issues and Options*[1] to clarify the issues surrounding financial sustainability and provide a framework for subsequent discussion and debate (in final draft form);
- convened a WHO-CVP-USAID Workshop on Financial Sustainability, 4-6 June 2001, with country teams that included representatives of the ministries of health and finance, and in-country partners from Bangladesh, Benin, Ukraine, and Zimbabwe;
- developed a financing "briefcase" to explore the range of financing options available to countries for immunization financing (in final draft form).

Financial sustainability – an updated definition

Traditionally, financial sustainability has been synonymous with "self-sufficiency", often applied to situations where external donors sought to induce developing country governments to mobilize domestic resources for activities that had previously been externally funded. The FTF considers that interpreting financial sustainability as "self-sufficiency" is inconsis-

[1] The draft paper, which was circulated widely for input and comment, is available in English, French, and Russian and is posted on the GAVI website, www.vaccinealliance.org.

tent with – and for many countries in direct opposition to – established GAVI milestones and objectives to increase coverage and introduce new vaccines.

The "new" emphasis currently being explored by the FTF is to move away from the single-minded attention to phasing-out external funding, and toward the question of how to structure the immunization financing package – and, equally importantly, how to use available resources more efficiently – so that sufficient funding is available on a reliable basis.

Based on consensus at the recent WHO-CVP-USAID Workshop on Financial Sustainability, the current working definition of financial sustainability reads:

Although self-sufficiency is the ultimate goal, in the nearer term sustainable financing is the ability of a country to mobilize and efficiently use domestic and supplementary external resources on a reliable basis to achieve target levels of immunization performance.[2]

This definition seeks to capture the following elements:

- fundamental importance of national commitment and funding for immunization with self-sufficiency being the ultimate goal;
- varying ability of countries to support their respective immunization programmes;
- focus on programme performance, rather than on inputs;
- importance of adequate and reliable resources to ensure that countries are able to meet immunization performance goals into the future;
- focus on the increasing resource requirements necessary to achieve GAVI goals;
- importance of using resources more efficiently.

Next steps

Recent work of the FTF has highlighted the need to recognize the multiple dimensions of financial sustainability[3] and for financial sustainability to become an integral part of future multi-year planning, with progress monitored as part of annual programme and financial reviews.

Over the coming months, the FTF will:

- refine key financial indicators (indicators will be few in number, easily interpretable, readily collected and will likely span several dimensions of financial sustainability);
- define global financing targets (FTF will likely be proposing two global financing targets – for countries and for donors – for consideration by the Board at a future meeting);
- draft guidelines for country sustainability plans using a wide consultative process.

[2] Immunization performance includes achieving current and future goals of access, utilization, quality, safety, and equity.

[3] Dimensions include sustained high demand for immunization services, efficient vaccine procurement and service provision, steady and sufficient funding for all programme elements, effective mobilization and management of supplementary external resources and long-term financing.

The FTF will also identify GAVI partners who will commit to supporting countries in the preparation and implementation of financial sustainability plans.

At the recent WHO-CVP-USAID Workshop, there was consensus that financial sustainability guidelines should require governments to demonstrate their national commitment to immunization. In some countries, this may be a plan to establish (if not already in place) a line item in the national budget with enacting legislation authorizing a minimum level of funding. For countries engaged in health sector reform and Sector Wide Approaches (SWAps), suggestions may be made as to how they can ensure that immunization programmes are protected, most likely through programme performance requirements.

The FTF will be submitting draft financial sustainability guidelines for consideration at the next GAVI Board meeting.

Annex 10
"Out-of-the-Box" – a financial think-tank for GAVI

Update

Objective: To accelerate the development, production scale-up, and distribution of three near-term vaccines (meningococcal A/C conjugate, pneumococcal conjugate and rotavirus) not only through strengthening and expanding the delivery of existing vaccines, but also by harnessing the complementary product expertise of both public organizations and private firms.

The introduction of cutting-edge vaccines and the creation of new vaccines for the developing world has been very slow for a variety of reasons. On the part of the public sector, financing constraints, low political visibility for preventive services and weak delivery systems have all contributed to the slow uptake of existing vaccines into national immunization schedules. In addition, concerns about the profit incentives motivating private industry have made the public sector wary of partnering with industry for the supply of new products. On industry's part, the historical unwillingness of the public sector to pay for vaccines, reinforced by the relatively small and uncertain revenues for "traditional" vaccines, have made vaccine-makers wary of investing in the development and production scale-up of new vaccines for developing country markets. The net result of these concerns is that few successful public/private partnerships exist, despite obvious need.

Public-private partnerships can only work if two basic conditions are met. First, both partners must understand the costs, risks and benefits driving the partnership. Second, both partners must be confident that the mechanisms or agreements that define the partnership protect each of their interests. For the public sector this means ensuring public investments result in more rapid development, expanded capacity and/or lower prices. For the private sector it means public "promises" translate into real financial commitments, minimizing the risk of late stage "changes of heart."

GAVI's goal is to address the barriers to rapid development, scale-up, and affordable prices through both the actions and partnerships of the public and private sectors. "Vaccine teams" comprised of technical experts and public and private manufacturers will jointly identify push-and-pull strategies that will overcome the identified gaps, recognizing that a combination of push-and-pull mechanisms will probably be necessary. The objective is to develop and ultimately implement product- and manufacturer-specific workplans which identify how and when specific strategies will be implemented for a defined end result.

In order to complement the immunization community's scientific and policy expertise, the Financing Task Force has convened a think-tank of creative financial experts called "Out-of-the-Box". This strategic and high-level working group includes a mix of experts from both the public and private sectors, including representatives from venture capital, ministries of finance, development agencies, the pharmaceutical industry and philanthropic foundations. The group will bring a unique set of skills to the public health community, including a better understanding of economic and financial motivations and markets, the creative

powers to break old patterns, and the personal and institutional credibility to back independent advice provided to the GAVI Board and other partners.

The overarching objective of the Out-of-the-Box group will be to create, improve upon, and validate new strategies and incentives to accelerate the development and use of priority health products for developing countries, beginning with an examination of the three near-term vaccines selected as GAVI priorities. The group will be asked to think broadly about how new financing mechanisms such as tiered pricing or off-shore production investment could be used to accelerate vaccine development.

Out-of-the-Box will also be asked to evaluate public-private proposals designed to overcome specific impediments to the efficient development, scale-up or use of the three new products, and to choose among one of four recommendations to GAVI partners:

- strong endorsement for the GAVI partners to identify funding,
- provisional endorsement, conditional on certain clarifications or modifications,
- re-review after additional analytic work, or
- strong reservations.

In evaluating the proposals, the Out-of-the-Box group will be asked to think broadly about the longer-term and non-financial impact of different finance arrangements, as well as the "fit" of the proposals with the overall goals of GAVI partners.

The existence of this core group of experts will bring new and creative ideas to our thinking, add rigour to our process, and provide the high-level validation which will be useful in gaining the buy-in of the immunization community.

On behalf of GAVI and the Financing Task Force, Mr James Wolfensohn, President of the World Bank, has invited the following individuals to join the Out-of-the-Box group. They have all accepted:

1) Ms Patty Stonesifer, Co-chair and President, Bill and Melinda Gates Foundation
2) Sir Richard Sykes, Non-Executive Chairman, GlaxoSmithKline
3) The Honourable Dr Katele Kalumba, Minister of Finance of Zambia
4) Mr Geoffrey Lamb, Director, World Bank
5) Dr Matthias Bekier, Principal, McKinsey & Company
6) Mr Paul Klingenstein, General Partner, Aberdare Ventures
7) Dr Seth Berkley, President and CEO, International AIDS Vaccine Initiative
8) Dr Mohamed A. El-Erian, Managing Director, Pacific Investment Management
9) Mr G. Stephen Burrill, CEO, Burrill & Co.
10) Dr. A. Richard Jefferson, PhD., Executive Director and Chief Research Scientist, Cambia

The Out-of-the-Box group will be convened twice yearly to offer their insight into GAVI projects. In addition, individual members may be asked to provide occasional inputs on specific topics or questions in which they have a particular expertise or interest. Out-of-the-Box will be in existence for three years, with the possibility of extending its life for an additional two years.

Annex 11
User fees and financing essential immunization services

GAVI policy statement

Beginning in September 2002, countries that have received support from GAVI and The Vaccine Fund will be submitting plans to the GAVI Board indicating how they will assure the long-term financial sustainability of improved immunization programmes. These financial sustainability plans are to be signed by the minister of finance in each country.

The GAVI Financing Task Force (FTF) is currently facilitating a process of drawing upon partners and countries to develop financial sustainability guidelines for consideration by the GAVI Board. In the interim, however, there are indications that some countries are proposing immunization user fees[1] as a means to finance the introduction of new vaccines and improved immunization programmes, as outlined in their applications to GAVI/The Vaccine Fund.

In 2000, the FTF undertook a major review[2] of all information and documentation on user fees for immunization and preventive health services. Research findings, multilateral agreements and policies of the World Bank and United Nations agencies all indicate that user fees discourage people from seeking vaccination for themselves and their children and are a disincentive to the utilization of preventive health services in general.

In addition to the deleterious effect of user fees on people's decisions to use appropriate preventive health services, user fees do not support national and international goals for more effective immunization systems and expanded vaccine coverage. This finding flows from the following:

- The positive externalities/benefits of immunization to the wider community justify public expenditure to promote widespread protection against disease and to stop disease transmission. As such, immunization programmes should be a high priority for national government investment.
- One principal and positive externality – protecting unvaccinated individuals through decreased disease transmission – can only be achieved with high levels of immunization coverage.
- There is no national or regional data to demonstrate that user fees help achieve high levels of routine immunization coverage.

[1] User fees are formal charges made by the public health service to the end consumer in exchange for immunization services. The purpose of user fees is to increase resources available to fund immunization programmes.

[2] England, S., Kaddar, M., Nigam, A., and Pinto, M. *Practice and policies on user fees for immunization in developing countries.* Geneva, World Health Organization, 2001 (unpublished document WHO/V&B/01.07; available on request from the Department of Vaccines and Biologicals, World Health Organization, 1211 Geneva 27, Switzerland.

- Vaccination is a preventive health intervention, and is more sensitive than curative services to the discouraging effects of user fees.
- Policies exempting the poor from user fees are difficult to administer.

Given the aforementioned concerns and the importance of conveying an interim message to countries, the FTF requests the GAVI Board to issue a policy statement to the following effect:

The GAVI Board recognizes that countries are exploring a variety of mechanisms to fund essential and routine immunization services. User fees have been shown to be a disincentive to the utilization of preventive health services including immunization, in particular. The GAVI Board therefore recommends that, in the absence of compelling country or regional data unequivocally documenting their value, user fees should not be levied in publicly financed national immunization services.

Annex 12
The Vaccine Fund

Supplemental assistance to support the introduction of new vaccines in countries with more than 80% DTP3 coverage

GAVI policy statement

Country eligibility for support from The Vaccine Fund sub-accounts is partly defined through the use of DTP3 immunization coverage as a proxy indicator for the capacity of the national immunization programme to introduce a new vaccine. Current policy determines that countries with a DTP3 coverage above 80% at the time of approval for support from the new and under-used vaccines sub-account are not eligible for support from the immunization services sub-account.

The rationale for this is the assumption that these countries, in light of their high coverage, have the capacity and resources needed to introduce a new vaccine in a safe and effective manner (i.e., apropriate logistics and infrastructure, the means to train health workers, build public awareness and secure demand for the new vaccine, and update reporting tools and materials). It is also assumed that assistance through the provision of vaccine from The Vaccine Fund will catalyse local commitment and mobilize resources from government and inter-agency coordinating committee (ICC) partners.

During the initial period of GAVI country operations, several countries are reporting resource problems in conjunction with the introduction of new vaccines. The two main reasons for this are that:

1) there is a greater than anticipated need to upgrade the immunization delivery infrastructure, such as replacing an ageing cold chain or training new health staff; and

2) it is difficult to make additional funding available at local level in a timely manner, since the process of GAVI approval and vaccine allocation occurs more rapidly than the mobilization of additional funds from government and donors.

It is therefore proposed that The Vaccine Fund allocate additional resources to this group of countries to ensure safe and effective introduction of new vaccines, in accordance with the following principles:

1) The Vaccine Fund will allocate a fixed amount of US$ 100,000 to all countries with DTP3 immunization coverage above 80%, upon approval for support from the new and under-used vaccines sub-account.

2) The aim of this additional support from The Vaccine Fund is to bridge the resource gap at the time of vaccine introduction and allow critical activities in the national vaccine introduction plan to be conducted in a timely manner. The government and ICC partners are expected to make additional resources available to ensure safe and effective introduction of vaccines nationwide.

3) Disbursements will be taken at the global level from the immunization services sub-account. They will be administratively handled in a similar manner to other disbursements from this sub-account. The ministry of health and ICC partners will be responsible for overseeing the use of these funds for vaccine introduction activities.

4) Countries approved for support in earlier rounds will be notified and additional support will be allocated on a retroactive basis.

5) At present, 20 Fund-eligible countries have a DTP3 coverage above 80%. Assuming that all of these countries will be approved to introduce one new vaccine, the proposed additional support could cost in the vicinity of US$ 2 million.

Annex 13
Developing-Country Vaccine Manufacturers' Network

Slide presentation

Dr Luis Herrera, Director General, CIGB, Cuba

Presentation at the GAVI Board Meeting London, June 2001

Slide 1: DCVMN: Who are we?

- Formed in November 2000.
- Seven-member steering committee.
- Full members are developing-country vaccine manufacturers (public and private), located in countries with fully functioning national regulation authorities (NRAs), and producing vaccines which meet WHO standards for sale by UN agencies. Or, if not, the manufacturers have taken demonstrable steps towards meeting WHO standards.

  Quality is key.
- Vaccinology institutions (WHO, IVI, RIVM) are resources for technical support for the network. WHO helps with network coordination and is the gathering point for production information.

Slide 2: Distribution by source of vaccines purchased through UNICEF tenders

	Number of pre-qualified vaccine manufacturers[1]	UNICEF supply specific[2] to Global Fund purchase	UNICEF supply for basic EPI vaccines, excluding OPV
Industrialized country vaccine manufacturers	12	73%	36%
Developing country vaccine manufacturers	9	27%	64%
Total	21	100%	100%

1 Not all pre-qualified vaccine manufacturers submit bids to UNICEF tenders.
2 HepB, Hib, DTwP-HepB, penta, yellow fever.

Slide 3: From the Meeting Report of DCVMN, 26-27 April 2001, Bandung, Indonesia

- For GFCV-funded vaccines, developing-country vaccine manufacturers (DCVM) receive, at this moment, a low fraction of the international supply contracts: about 90% of the value of total supplies is used to purchase combo's – DTP-HepB, DTP-HepB-Hib or Hib – from the pharmaceutical industry. The remaining 10% represents HepB purchased from, amongst others, producers in developing or middle-income countries. (An initial amount of approximately US$130 million was allocated by the Fund early in 2001.)
- UNICEF expects that, after allocation of remaining funds, expenditure on GFCV-funded vaccines (Hib, rHepB and DTP-based combo's) will eventually reach up to 30% for DCVM.

Slide 4:	Status of producers

WHO-qualified	In the qualification process
• Serum Institute of India • Lucky Goldstar, Korea • Cheil Jedang, Korea • Green Cross Vaccine, Korea • BioFarma, Indonesia • Institut Pasteur Dakar, Senegal	• Center for Genetic Engineering and Biotechnology, Cuba • Shanta Biotech, India • Biological E, India • Butantan Institute, Brazil

Slide 5:	Pre-qualified vaccines currently available from DCVMs

- BCG, DT, DTwP, OPV, TT, M, MR, Hep B, YF .
- Made available through UNICEF and WHO and have private export markets .
- Most are expanding capacity and adding new technologies including DTwP based combination vaccines and Hib.
- Have R&D efforts toward rotavirus, pneumococcus, and other vaccine needs.

Slide 6: DCVM production capacities for different vaccines (million of doses)

Vaccines	Current	Potential
DTwP	347	606
Rec. Hep B (yeast)	283	650
Rec. Hep B (CHO)	2	4
Hib	15	22
Typhoid	5.2	39
Cholera	8	11

Slide 7: Where are we from?

Full members of the Network[1] are in the following countries:

- Brazil
- Cuba
- China
- India
- Indonesia
- Mexico

[1] Additional manufacturers who meet requirements are being invited to join.

Slide 8:	DCVMN goals

1. To provide quality vaccines at affordable prices to the developing world. This includes vaccines that are needed in developing countries and also vaccines in which industrialized nations and, possibly, big pharma have a limited interest.
2. To obtain recognition that developing-country vaccine producers have an essential role in assuring availability of vaccines to immunize every child.

Slide 9:	New vaccines under development

- Combinations:

  DTP-HB
  DTP-Hib
  DTP-HB-Hib
  BCG-HB
  Measles-Japanese encephalitis
  Measles-Mumps-Rubella

- Conjugated

  Meningitis A-T
  Meningitis C-T
  Thyphoid-T
  Hib-T
  Pneumococcus

- Recombinant/chemical synthesis

  BCG-DPT
  BCG-Schistosoma
  Cholera
  Hib
  HIV
  Pneumococcus PsaA PspA
  Schistosoma
  TB
  Malaria

Slide 10: DCVMN-specific objectives

- Manufacturers who meet WHO standards and product-specific requirements will offer all EPI vaccines, including HepB and Hib, at affordable prices.
- Provide a platform for the development of priority projects, with guidance from WHO, on global vaccine needs in line with national needs (DTwP-based combination vaccines, under-utilized vaccines for developing countries, and coordination of research and development efforts and clinical trials).
- Provide a repository of information, such as an inventory of current and potential production capacities, and facilitate information exchange amongst members.
- Provide training on vaccinology.
- Act as facilitator in technology transfers.
- Provide independent laboratory support for members' projects and coordinate regulatory requirements.

Slide 11: What can the DCVMN do for GAVI?

- Continue to provide high-quality traditional vaccines to developing countries as the backbone to immunization programmes.
- Speed the provision of quality DTwP-based combination vaccines for developing countries, thereby contributing to the sustainability goal.
- Contribute to the R&D efforts and the manufacture of vaccines that are being developed specifically for use in developing countries.
- Help strengthen other local manufacturers.

Slide 12: How can GAVI support the DCVMN?

- Purchase guarantees for pre-qualified vaccines.
- Support business agreements for IPRs.
- Strengthen the NRAs in many developing countries.
- Provision of a facilitator to better execute agreed technology transfers.
- Relieve capital constraints:
  - financing needed to expand production into other desired vaccines (support of R&D) such as rota and pneumo.
  - assistance, when necessary, for clinical trials.

Annex 14
GAVI and The Vaccine Fund

Annex 14.1
Relationship between GAVI and The Vaccine Fund

Background

- GAVI and The Vaccine Fund have evolved in a highly interconnected manner, contributing greatly to the efficiency and focus of our work (see Table 1). However, the close yet separate relationship has given rise to confusion about the relative roles, and inconsistency in messages conveyed to internal and external audiences. In addition, without more clearly defined roles there is a potential for duplication of efforts, competition relating to promotion and public relations, diverging operations and fragmentation of efforts. (See Annex 14.2).

- The Working Group and Executive Committee of The Vaccine Fund considered three directions for future development of the Alliance and The Vaccine Fund: a merger of operations and supervision; a clearer separation of roles and identities, or continuing the independent yet tightly linked structure. Of those options, the distinct but linked structure was considered to be the most effective model for achieving the objectives of GAVI and The Vaccine Fund.

- The Branding Group was therefore authorized to develop brand identities for both GAVI and The Vaccine Fund, incorporating techniques that convey the linked structure.

Recommmendations

1) Endorse the name change from the "Fund" to "The Vaccine Fund".

2) Adopt separate but mutually reinforcing logos and graphic identities that convey the relationship (e.g., GAVI – Partnering with The Vaccine Fund; and The Vaccine Fund – Partnering with GAVI). On completion of the branding exercise, the two Secretariats will jointly develop and monitor graphic guidelines.

3) Rapidly disseminate the outcome of the branding study on GAVI and The Vaccine Fund among the different levels of the GAVI partners in order to promote consistent messages throughout the GAVI network.

4) Increase links through common supervision of the two Secretariats by the Working Group and the Executive Committee through joint meetings convened annually or more frequently as appropriate; hold joint meetings of the staff of the two Secretariats as appropriate.

Table 1: Division of work between GAVI and The Vaccine Fund

#	Tasks	The Vaccine Fund[1]	GAVI[2]	GAVI partners and task forces
1.	Policy development		++ WG	+ (WHO)
2.	Country proposal development			+++ (ICC)
3.	Proposal review process		++ S	+
4.	Procurement and distribution of vaccines			+++ (UNICEF)
5.	Disbursement of funds to countries		+ S	++ (UNICEF)
6.	Monitoring of activities in countries		++ S	++ (TFCC, RWGs)
7.	Financial projections and monitoring	++	+	
8.	Resource mobilization for Vaccine Fund and GAVI-related partner activities	++	+ S	+
9.	Global advocacy and communications	++	+ S	+ (ATF)
10.	Country-level advocacy and communications			+++ (ATF, TFCC, RWG, ICC)

WG Working Group
S Secretariat
TFCC Task Force on Country Coordination
ATF Advocacy Task Force
RWG Regional working groups
ICC Inter-agency coordinating committees

1 To execute functions of the Fund Board.
2 To execute functions of the GAVI Board.

Annex 14.2
Collaborative mechanisms for disbursement of support to countries

The Global Alliance for Vaccines and Immunization,GAVI, has established several mechanisms to help meet its objectives. One important mechanism links two major steps in the GAVI process – on the one hand, the GAVI Board's endorsement of programmes proposed by governments and, on the other, disbursement of funds to support the programmes endorsed by the GAVI Board. This note describes that mechanism in general terms.

The mechanism is established in the Relationship and Contribution Agreements between the Global Fund for Children's Vaccines (the "Global Fund") and UNICEF (as custodian of the Global Fund Trust Account at UNICEF), and in the Contribution Agreement between contributors to the Fund and UNICEF (as custodian of the Global Fund Trust Account at UNICEF). As these documents indicate, contributions to support programmes to be endorsed by the GAVI Board can be transferred to the Global Fund account or the Global Fund Trust Account at UNICEF.

Two fundamental principles of the Alliance are the centrality of the GAVI Board, and the rigour of the process of developing, reviewing, and endorsing programmes proposed by governments.

The GAVI Board is composed of representatives of the members of the Alliance. It is the highest body of the Alliance and represents the allies' commitment to ensuring the success of this initiative. Its role is, inter alia, to consider the programmes that governments propose to the Board for endorsement. Each programme will have been developed by a government, in consultation with its national inter-agency coordinating committee (ICC) or equivalent collaborative mechanism.

By the time the programmes are formally referred to the GAVI Board by the GAVI Secretariat, they will have been subject to vigorous review by a panel of independent public health experts. The GAVI Board will consider programmes on a regular basis – at least twice a year. It is anticipated that most programmes that are formally presented to the Board, following the review process, will be endorsed. Endorsement by the Board constitutes endorsement by the Alliance of the programme itself, the projected budgets and the statement of the necessary support (as outlined in the submitted government programme documents).

Once a programme, together with its budget and support statement, is endorsed by the Alliance, the Secretariat will advise both the Global Fund and UNICEF (as custodian of the Global Fund Trust Account at UNICEF).

The Global Fund is an integral part of the GAVI process. As its incorporating documents set forth, the Global Fund was organized in response to the establishment of GAVI "to provide financial support for the purchase of newer and under-utilized vaccines and the means to deliver such vaccines to the children of the world … and … to coordinate its charitable efforts with GAVI and … to provide funds to purchase vaccines for programs that form part

of the GAVI members' immunization initiatives". The Board of the Global Fund will be composed of independent individuals with distinguished records who serve in their personal capacities; it is currently guided by an interim board. The members of the Interim Board are Mark Kane (Chair), Bill and Melinda Gates Children's Vaccine Program; Tore Godal, GAVI; Chip Lyons, US Fund for UNICEF; Jacques-François Martin, the Global Fund; Gordon Perkin, Bill & Melinda Gates Foundation. Decisions are being made by consensus, often by teleconference. In order to secure efficiency, the Board of the Global Fund will delegate disbursement responsibilities to an executive committee.

The Board of the Global Fund will take note of the programmes endorsed by the GAVI Board and determine the funding support of the Global Fund for these programmes, based on all relevant factors including total availability of resources. It is expected that there will be close consultation between the GAVI Working Group and the Global Fund – this will ensure that factors that might be relevant in the deliberations of the Board of the Global Fund are known to the GAVI Working Group. As a further sign of the collaboration between the GAVI mechanisms and the Global Fund, the Alliance has invited the President of the Global Fund to become a member of the GAVI Working Group.

The Global Fund's support will be made available through transfer into the Global Fund Trust Account at UNICEF. Once the Global Fund has transferred funds to the Global Fund Trust Account at UNICEF to support a particular programme, UNICEF will draw on those funds and on the funds already deposited in that account, in order to provide support for the programme. UNICEF will make disbursements from the Global Fund Trust Account at UNICEF in accordance with budgets endorsed by the GAVI Board for programmes and projects endorsed by the GAVI Boards.[1]

These mechanisms have been designed to ensure that GAVI's goals are achieved as quickly as possible, and in a sustainable way. The mechanisms have been developed with a consciousness of the goodwill and commitment of all the members of the Alliance and those who are part of the GAVI process; we are confident that they will achieve all that they have been designed to achieve, and more.

Current policies for disbursements:

- Countries with incomes of less than or equal to US$ 1000 gross national product (GNP) per capita are eligible for support from the Global Fund. Among these, special arrangements are being explored for the three largest countries : China, India and Indonesia.
- The three basic conditions for support are: a functioning inter-agency coordination committee (ICC) or equivalent collaboration mechanism; a recent assessment of immunization services; and the existence of a multi-year plan for immunization. In addition, countries are expected to follow safe immunization procedures, and have plans to improve safety if there is room for improvement.

[1] In the event that the Board of the Global Fund considers it is not in a position to support a programme or project endorsed by the GAVI Board, the two will confer to reach a resolution of any difference of opinion. It has been agreed that, recognizing the GAVI Board's overarching role as the highest body of the Alliance, if the two have not reached agreement within two months, the funds already deposited to the Global Fund Trust Account at UNICEF by all contributors will be disbursed, thus providing the support contemplated by the GAVI Board at the time it endorsed the programme or project in question.

- The Global Fund currently provides support for immunization services and procurement of new and under-used vaccines. A third sub-account for research is under consideration.
- Support from the immunization services sub-account will initially be eligible for countries with current DTP3 coverage of less than 80%. In order to provide contributions on a performance basis, the concept of "shares" has been developed, with each share representing the Fund's contribution toward immunizing one additional child (currently US$ 20). Shares are provided without conditions for the use of funds, but with strict requirements for performance and a reliance upon governments and ICCs (or equivalent) to set goals and monitor progress.
- The sub-account for new and under-used vaccines will initially be used to purchase vaccines against hepatitis B (hepB), *Haemophilus influenzae* type b (Hib) and yellow fever, and associated safe injection materials for countries with national DTP3 coverage of more than 50%.
- The development of these policies has been an integrated process, achieved through an overlapping of memberships between the two Boards and/or the GAVI Working Group. It is thus anticipated that policy development, including eligibility criteria for fund disbursements, will continue as an integrated process, and that the GAVI Board will make its decisions in the presence of updated information on the financial resources of the Global Fund.

Annex 15
List of participants

(5th GAVI Board Meeting, June 2001)

Board Members

Chair

1. Dr Gro Harlem Brundtland, Director-General, WHO
2. *Alternate*: Ms Namita Pradhan, Senior Policy Analyst, DGO, WHO

Bill & Melinda Gates Foundation

3. Mr William H. Gates Sr., Co-Chair and CEO, the Bill & Melinda Gates Foundation, USA

Foundations

4. Dr Tim Evans, Team Director, Health Sciences Division, Rockefeller Foundation, USA

Developing Country Governments

5. Dr Fatoumata Nafo-Traore, Minister of Health, Mali
6. Mr Lyonpo Sangay Ngedup, Minister of Health and Education, Bhutan

Industrialized Country Governments

7. Dr Els Borst-Eilers, Deputy Prime Minister and Minister of Health, Welfare and Sport, the Netherlands
8. *Alternate*: Mr Jacob Waslander, First Secretary, Permanent Mission of The Netherlands to the UN Office at Geneva
9. Ms Maria Minna, Minister for International Cooperation, Canada
10. *Alternate*: Ms Margaret H. Ford, Director General United Nations and Commonwealth Programmes
11. Dr Sigrun Mogedal, State Secretary, Norway
12. *Alternate*: Dr Rune Lea, Senior Adviser, Norad, Norway

Incoming Board Member:

13. Ms Clare Short, MP, Secretary of State for International Development, United Kingdom

14. *Alternate*: Dr Julian Lob-Levyt, Department for International Development

Non-governmental organizations

15. Dr Mark Kane, Director, Bill and Melinda Gates Children's Vaccine Program, USA

Research and development

16. Dr John LaMontagne, Deputy Director, NIAID, National Institutes of Health (NIH), USA

Technical health institute

17. Dr David W. Fleming, Deputy Director for Science and Public Health, Centers for Disease Control and Prevention (CDC), USA

The World Bank

18. Mr James Christopher Lovelace, Director, Health Nutrition and Population, The World Bank

UNICEF

19. Ms Carol Bellamy, Executive Director, UNICEF

20. Dr Suomi Sakai, Chief, Immunization Activities, UNICEF

Vaccine industry – developing country

21. Dr Luis Saturnino Herrera Martinez, Director-General, Center for Genetic Engineering and Biotechnology (CIGB), Cuba

Vaccine industry – industrialized country

22. Mr Jean-Jacques Bertrand, Chairman and Chief Executive Officer, Aventis Pasteur, France

World Health Organization

23. Dr Yasuhiro Suzuki, Executive Director, Health Technology and Pharmaceuticals, WHO

The Vaccine Fund

24. Mr Jacques-François Martin, President, The Vaccine Fund

25. Mr Charles Lyons, President, US Fund for UNICEF, USA

26. Dr Gordon Perkin, Bill & Melinda Gates Foundation, Seattle, USA

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27. Ms Caroline Akim, EPI Manager, Ministry of Health, Tanzania
28. Ms Amie Batson, Senior Health Specialist, the World Bank
29. Dr Paul Fife, Health Adviser, UNICEF
30. Dr Tore Godal, Executive Secretary, GAVI Secretariat
31. Ms Jackie Keith, Assistant Vice President, Wyeth-Ayerst Labs, USA
32. Dr Steve Landry, Technical Advisor, Child Survival, Population, Health and Nutrition, USAID, USA
33. Ms Heidi Larson, Senior Communication Adviser, UNICEF
34. Dr Mike Levine, Director, Center for Vaccine Development, University of Maryland School of Medicine, USA
35. Mr Michel Zaffran, Programme Manager, Vaccines and Biologicals, WHO

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37. Dr Stephen Cochi, Centers for Disease Control and Prevention, USA
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39. Mr Richard Greene, Chief, Child Survival Division, USAID, USA
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46. Ms Millicent Obaso, Manager, Africa Initiative, American Red Cross, USA
47. Mr Bo Stenson, Principal Officer, GAVI Secretariat
48. Mr Victor Zonana, Vice President, The Vaccine Fund

Temporary Advisers (for specific agenda items)

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50. Ms Tracey Goodman, Polio Eradication Initiative, WHO
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