



Médecins Sans Frontières & Oxfam consultation
26 January 2010, Geneva, Switzerland

Improving access and stimulating vaccine development for use in resource-poor settings

Consultation summary

Introduction

Goals and objectives of the meeting

Introduction by Dr. Tido von Schoen-Angerer, MSF Access Campaign

- Médecins Sans Frontières (MSF) and Oxfam are in the process of developing new policy positions on vaccines. Outbreak response has always been a particular focus for MSF but the organisation is also highly committed to the introduction of new vaccines.
- There has been progress in increasing vaccine coverage and introduction of vaccines for Hepatitis B virus (HBV) and Haemophilus influenza type B (Hib) in recent years.
- Nevertheless, there are considerable limitations to the current model: new vaccines are not sufficiently affordable nor sufficiently adapted to developing country needs.
- The GAVI Alliance (GAVI) is facing an important financing shortfall which makes the issue of vaccine prices all the more important. Collective bargaining power, e.g. through the Pan-American Health Organization (PAHO) is no longer proving sufficient to achieve affordable prices for new vaccines.
- To address these challenges, significant adjustments and changes to current system might be necessary.

Context: Vaccines for the developing world - access and R&D

Presentation on the conclusions of an MSF/Oxfam commissioned paper on environment of vaccines access and R&D for the developing world by Paul Wilson, consultant.

- Over the past years there have been major successes in terms of vaccine coverage, new vaccines being introduced and developed:
 - Increase in basic immunisation coverage, although disparities remain
 - Introduction of additional vaccines in the Expanded Program on Immunization (EPI) package
 - Development of several important new vaccines
- But there are limitations to the current model:
 - The prices of some newer vaccines are still too high for most developing countries;
 - Some newer vaccines are not adapted to the medical needs and logistical constraints of developing countries; existing vaccines are developed with wealthy markets in mind; relying on hand-me-downs often results in vaccines that target the wrong serotypes, and/or come in the wrong presentations.

- The financing of developing country access to vaccines is under strain: GAVI is experiencing difficulties meeting its commitments and reaching its objectives, with a decline expected in special revenues from the International Finance Facility for Immunisation (IFFIm) after 2010 and with the effects of the economic crisis. In addition, most low-income countries still dependent on GAVI funding, and tiered pricing is showing limitations.
- There has been considerable delay in uptake of new vaccines in developing countries – the first pneumococcus conjugate vaccine (PCV) was licensed in 2000
- In terms of R&D, the challenges are that for first or better vaccines against “neglected” diseases, the private sector will not invest sufficiently in vaccines that don’t promise large markets;
- Possible solutions for access to more affordable vaccines:
 - Reducing the barriers and timelines to the entry of new suppliers by transferring technology and know-how; overcoming intellectual property barriers;
 - Streamlining regulatory pathways for “follow-on” vaccines;
 - Using pooled procurement mechanisms like PAHO’s to enhance bargaining power;
 - Developing forms of tiered pricing acceptable to middle-income countries;
 - Exploring mechanisms for de-linking product prices from R&D costs; e.g. by paying for the R&D upfront.
 - Finding sustainable funding for GAVI.
- Possible solutions for the development of adapted vaccines for the developing world:
 - Product development partnerships (PDPs) and partnerships like the Meningitis Vaccine Project (MVP) could be part of the solution;
 - “Pull” funding mechanisms, including prizes and enhancing the R&D capacity of emerging suppliers should be explored.
 - Answering the unanswered question of ‘who decides?’ - Governance & priority setting.

Roundtable I: **Challenges to the development of adapted and affordable vaccines - Case studies**

Heat-stable vaccine technologies:

Opportunities and bottlenecks for development, introduction, and adoption.

Presentation by Modibo Dicko, WHO

- Supply channels requiring cold-chain come with considerable challenges, particularly with newer vaccines which have larger volumes. Despite stability data, vaccines are still stored at 2 to 8 degrees.
- Based on country-level evidence, regulatory pathways and programmatic working group, the aim is to adopt a controlled temperature chain. The work on HBV, which is quite stable at high temperatures, was given as an example.
- The aim is that true vaccine stability is better reflected in prescribing information, to identify regulatory pathways and to encourage industry to carry out stability tests at higher temperature ranges & submit data to regulatory bodies.

Discussion:

- *The responses from companies regarding the inclusion of heat-stability in the R&D process.*
Some companies are very favourable; some already have heat-stability data but do not submit it as it's not required. Manufacturers may have access to stability data, but are

reluctant to take more risks than are currently required from a regulatory point of view. Refusing to make those data public means, for example, that even if a vaccine is stable at room temperature, it cannot be used outside the required temperatures.

- *Implementation of Controlled Temperature Chains.* Recognising the advantages of basing cold chain on true vaccine stability, it was discussed that too many different storage recommendations for different vaccines could create confusion. Programmatic guidelines should be sufficiently simple and easy to follow. Although company data support storage at room temperature, caution should be used when changing the temperatures required to store vaccines to avoid that logistics and local programmatic issues be negatively impacted.

Rotavirus and PCV:

Appropriateness of vaccines developed for global vaccine market

Presentation on by Rebecca Grais, Epicentre

- There is a lack of epidemiological data in certain regions, compounded by large geographic variability in rotavirus prevalence and mortality in sub-Saharan Africa.
- Current vaccines are not well adapted to sub-Saharan Africa. WHO prequalified vaccines have proven efficacy mainly against the G1-G4 and G9 serotypes which represent only 57% of the circulating strains in sub-Saharan Africa.
- Additional challenges include the narrow age window to complete the course of vaccination and storage volume in already strained cold chains. More adapted formulations such as oral film should be further developed and explored.
- The pneumococcal conjugate vaccine may be one of the most important new vaccines to address disease burden in crisis affected populations. However, administering the recommended three doses is not feasible through mass vaccination of crisis affected population. The concept of a planned study to compare the efficacy of one, two or three doses was presented.
- Needed characteristics of new vaccines for developing countries include: to be heat-stable; have low space requirements; require low dosage; cover context relevant serotypes; be efficacious in a range of immune profiles (e.g. malnourished children) and ideally have needle-free delivery.

Discussion:

- *Difficulty of rotavirus diagnosis is a challenge.* Attributing cases of diarrhoea to rotavirus in the absence of easy-to-use tests makes the needed research difficult. This lack of diagnostic tests is also a problem with other diseases such as typhoid.
- *The film formulation.* An orally resolvable film formulation would be a great improvement and its further development for rotavirus should be encouraged. What you put on (in terms of serotypes) the film will be the question. These questions and gaps have come up late in the development process because the existing rotavirus vaccines were developed for wealthy countries despite the fact that the majority of beneficiaries are in the developing world.
- *Live Rotavirus vaccines are not necessarily the most effective.* Other types of Rota vaccines could be developed.
- *PCV vaccination in emergency settings.* Participants considered the planned study as very important. Questions were raised why such an important study had not already been done by those financing and promoting the introduction of PCV. Suggestions were made to significantly simplify the study design.
- *Pneumo Advance Market Commitment (AMC).*
 - Given a tail price of up to US\$3.50 per dose, questions were raised if countries will be able to afford and continue to provide this vaccine once GAVI support ends.

- The current system where a country's co-payment is the same regardless of which PCV it chooses, encourages the drive to constantly increase the number of serotypes regardless of public health benefit and long term sustainable cost; in the current system there is no incentive for developing countries to choose anything less than the "Mercedes", i.e. the PCV with most serotypes.
- *Is the perfect the enemy of the good?* Is this rush to add more serotypes justified? Could there be serotype adapted but more sustainably priced vaccines specific for developing countries? This would require a change in the approach to vaccine development. And it raises the question - how 'good' does 'good' have to be?
- *Decisions based on marketing returns rather than medical need.* PCV-9 is a good case study as the development of this product, which would have met the WHO target product profile, was ended despite excellent results in developing countries. How can we change this dynamic which leads to sub-optimal decisions?
 - What would have been the price advantage of PCV-9 over PCV-10 or -13?
 - What is the optimum number of serotypes given the risk of serotype replacement?
 - Can these questions be addressed by developing country research institutes? How to incentivise developing country manufacturers to solve these problems?

Roundtable II: Access to newer vaccines

Opportunities and challenges with introduction of newer vaccines:

What is needed from the next generation of vaccines?

Presentation by Samba Sow, Director Mali Center for Vaccine Development

- In Mali's experience in introducing the Hib and the pentavalent vaccine, there is a need to quantify local disease burden, with good routine surveillance data at country level.
- Measuring the impact of vaccination was found critical to convince decision makers and donors.
- Challenges faced: funding delays, ensuring adequate vaccine supply and sustainable pricing; and vaccine transition (step-wise approach increases risk for overlap and confusion). Training, supervision and assessing cold-chain requirements in advance were deemed essential.
- Specific challenges for pneumo introduction in Mali include: need to understand and monitor serotypes prevalence; issue of price. One of the specific challenges for rota introduction is communication that the vaccine does not prevent all diarrhoea.
- Countries face important questions in balancing opportunities from new vaccines and challenges and possible disturbances. It is unlikely that a country can handle all priority vaccines at once. Countries therefore need sufficient data on national disease burden to allow prioritisation of which vaccine to introduce first. In Mali practical challenges will be faced on training, cold chain logistics and avoiding disturbances of ongoing campaigns (polio, measles, tetanus).
- Price and sustainability are a concern, as GAVI requires increasing country co-payments and proportion of immunisation cost on the health budget is increasing. Right presentation (reasonable cold chain volume, not freeze sensitive, oral delivery if possible etc) will also facilitate introduction.
- Countries need mechanisms and processes for prioritisation based on disease burden.

Discussion:

- *The need for increased capacity for surveillance, analysis and decision-making regarding setting priorities at the local level.* Does current Accelerated Vaccine Introduction Initiative (AVI, a Johns Hopkins/US Centers for Disease Control/Path consortium) meet country needs?
- *Introducing one vaccine at a time.* Countries need to be closely involved in decisions on how to prioritise vaccine introduction. Instead of ‘one fits all’ decision, each country need to prioritise based on disease burden. Surveillance has however been a problem in the past, in particular laboratory support.

New regulatory pathway for vaccine registration

Presentation by Gillian Chaloner-Larsson

- Since the early 1990s, WHO has been active in training and developing expertise of national regulatory authorities in developing countries, both in vaccine manufacturing countries and in vaccine procuring countries.
- In 1995, a public Manufacturers Consortium meeting took place to discuss cooperation among public manufacturers for improvement of manufacturing in developing countries and emphasized training of National Regulatory Agencies (NRA) as a priority. The Developing Country Manufacturers Network (DCMN) which includes public and private manufacturers was created.
- The six critical functions for vaccine regulation and corresponding indicators were established in 1996. The Global Training Network started in 1997 to train NRA staff from many countries. The WHO Prequalification programme was created to evaluate vaccines against WHO recommendations to be eligible for sale to United Nations Agencies.
- NRA assessment began based on critical functions and corresponding indicators to determine if an NRA is “fully functional”. NRA must be fully functional for manufacturers in the country to obtain WHO prequalification for one or more vaccines.
- In 2002, there was recognition that new regulatory pathways for licensing would be needed for vaccines needed in developing countries manufactured by developing country manufacturers.
- WHO Initiative for Vaccine Research (IVR) started contract manufacturers database to identify, assess and register several dozen contract manufacturers with capacities in one or more aspects of good manufacturing practices (GMP) that could be contracted to aid vaccine developers to manufacture suitable GMP clinical trial material for phase I and II clinical trials.

Discussion:

- *Convergence of regulatory standards.* Is this unambiguously a good thing? Do we want regulatory authority standards in developing countries to be the same as in developed world? Some participants supported a more consistent international framework while others stressed that epidemiology of disease is different in different countries so there must consideration of risk/benefit in order to make a decision on which requirements are put in place. One participant suggested that standards on manufacturing and pre-clinical data should be the same but that requirements for clinical data and risk/benefit decision would differ according to context. There was a concern expressed that today most standards are driven by the U.S. FDA or EMEA and developing countries such as Brazil are emulating those requirements - this is a real concern.
- The WHO Prequalification mechanism is very important for developing countries that don’t have a functioning national regulatory authority; they rely heavily on this mechanism to ensure that vaccines used in their countries meet international WHO/ICH quality standards.

Financial sustainability of the current model to introduce new vaccines: What is needed to create a more enabling environment?

Presentation by Lidija Kamara, WHO

- GAVI has had a huge positive impact in vaccine introduction in the poorest countries, but the affordability of current vaccines (e.g. Hib) for national governments is far from assured. On average, there is a \$4 funding gap per infant to reach goals of scaling up and completing the HBV and Hib agenda.
- Many of GAVI's financing assumptions such as vaccine price reductions and ensuring financial sustainability of GAVI's catalytic funding have not been realised as expected. Given the price of new vaccines, the current country co-financing equates to only a small fraction of total vaccine costs. The price decrease of the pentavalent vaccine was slower and less steep than expected.
- Countries with the lowest co-financing levels and least ability to pay have introduced the most expensive vaccines. These same countries are the ones most reliant on external funding.
- There are many challenges linked to the accelerated uptake and sustained introduction of new vaccines (e.g. PCV, Rota, HPV). Further innovation and investments are needed to impact vaccine supply and price, and significant amounts of funding are required (external and national) to reach internationally accepted coverage objectives.
- Tiered pricing is simple in theory but complex in practice. Low-income countries are charged reduced prices through bulk procurement systems (UNICEF, PAHO) which boost access to vaccines, while providing manufacturers with a profitable market in richer markets. But this system has been performing less well with new more expensive vaccines. It is also clear that prices are the result of multiple factors and not determined solely by the country income level.
- The entry of emerging manufacturers has been effective in bringing down the price of traditional vaccines and it is to be seen if the same can be achieved for newer vaccines. The question is how the international community can contribute to building an enabling environment to promote competition, better response to priority needs and a health vaccine market.

Discussion:

- *Distorting effects of co-financing.* The co-pay is discriminating against new products that are more affordable and is not creating any incentive for cheaper vaccines. This is because of the amount a country has to co-pay for a very cheap or a very expensive vaccine. Note that GAVI is currently revisiting its co-financing policies.
- *GAVI role in health systems strengthening (HSS).* GAVI is a partner with the World Bank and Global Fund which is being financed by donors to support a new HSS joint instrument with an envelope of \$1.1 billion over four years. Participants questioned the emphasis on HSS at a time where funding of commodities was not ensured and stressed that both need to be simultaneous.

Roundtable III: Existing and new ways to support technology transfer and implementation science

Different current and possible models

Presentation by Marie-Paule Kieny, WHO

- WHO influenza vaccine technology transfer programme: WHO's role was to facilitate acquisition of influenza vaccine production capacity in developing countries by supplying funds and facilitating technology transfer to 11 developing country producers. A royalty-free licence was negotiated by WHO and a sub-licence was provided to three developing country vaccine manufacturers (China, India, Thailand). The success of technology transfer also strongly depends on the commitment and quality of relation between the people involved.
- By involving a number of different inventors/developers and a number of different users, a technology hub approach offered an alternative to more traditional tech transfer from one technology owner to one user.
- There is an expanded manufacturing capacity in developing countries, but with consolidation in the industry their long-term independence remains uncertain.
- A number of assumptions may need to be revisited:
 - "predictable demand will automatically lead to reduced prices";
 - "vaccine price is not important as long as the donor community is paying ";
 - "technology transfer must always be a stepwise approach, starting with fill/finish"

Project-managed approach: The Meningitis A conjugate example

Presentation by Marc Laforce, PATH

- The MVP project was created in June 2001 through a grant from the Bill & Melinda Gates Foundation. It is a 10 year partnership between WHO and PATH to eliminate epidemic meningitis as a public health problem in sub-Saharan Africa through the development, testing, licensure, and widespread use of conjugate meningococcal vaccines.
- This was done with the aim of eliminating the 15-18 year time lag between North and South seen with the introduction of HBV and Hib vaccines.
- The cost of the vaccine was considered one of the most significant challenges identified by countries - which is not surprising given that meningitis belt countries are among the poorest in the world. Therefore the target price was set as \$0.50 per dose.
- The decision was made to pursue the development of a monovalent A vaccine using a push strategy. No agreement could be reached with major vaccine manufacturers. Therefore a consortium was created to identify raw materials, license a conjugation method and find a vaccine manufacturer willing to accept technology transfer and market the conjugate vaccine at a for-profit-price of less than \$0.50 per dose. The Serum Institute of India (SII) accepted.
- Intellectual property was managed by setting up confidentiality agreements and material transfer agreements with the U.S. FDA/ Center for Biologics Evaluation and Research (CBER), and licensing agreements with the U.S. National Institutes for Health.

Discussion:

- *Role of public sector.* The MVP was facilitated by the fact that the know-how for conjugate meningitis vaccines already existed and was held in the public sector.
- *Costs.* Clinical trials have been proven to be the most expensive part of the process. The total development cost will be \$50-60 million; SSI added about \$15-20 million; when adding surveillance and delivery systems the global cost rises to about \$100 million.
- *Annual production* will be around 50 million doses per year. Another manufacturer may manufacture the Men A conjugate, although given the current low price, this was thought to be unlikely.

Netherlands Vaccine Institute (NVI) experience & concept of central technology hub

Presentation by Jan Hendriks, NVI

- Since the 1990's NVI has provided technology transfer to developing countries on EPI vaccines (DTP, measles, polio) and Hib conjugate vaccines. More recently NVI has initiated projects with WHO on inactivated polio vaccines and influenza vaccine.
- Patent and proprietary know-how issues have complicated access to Hib technology.
- Other challenges for the Hib technology transfer included: regulatory barriers to the use of alternative conjugate technology; ethical issues which complicate the use of alternative conjugate technology (as it is difficult to justify clinical trials with these conjugates in the presence of licensed Hib vaccines which are highly safe and effective); the presence of competing vaccines, which meant donors were not willing to fund the project as this would have been seen as unfair competition.
- The creation by GAVI of a market for Hib conjugate vaccines, and WHO's recommendation to incorporate Hib vaccine in all infant immunisation programmes have enabled the development of a patent-free production process for the large-scale production of Hib conjugate vaccine which could be scaled up. Technology transfer to developing countries ensures a sustainable supply of affordable and quality vaccines.
- More recently NVI has created a tech transfer platform in collaboration with WHO for egg-based production of the pandemic influenza vaccine.
- The hub-concept with WHO on flu and polio bears promise, and could be expanded to include other products.
- Following a decision by the Dutch Ministry of Health, NVI production will be privatised by 2012. The challenges for NVI and its capacity to stay engaged in technology transfer will be to maintain access to production infrastructure and R&D capable to transform research into practice.

Discussion:

- *The role of NVI during scale up.* NVI handles the pilot phase and gives back-up support.
- *The future of NVI is uncertain.* The production facilities will be/are currently being sold to the private sector, but NVI does hope that they can maintain the vaccine development parts. Funding from the Dutch government has been winding down. This is particularly unfortunate as NVI is one of the few public institutes still involved in vaccine development and production.
- There would be potential to organise tech transfer to developing country manufacturers through a network of the EU-based vaccinology institutions like NVI. This idea could be presented to policy makers.
- *Intellectual property held in the public sector.* Universities should be asked to not give exclusive licences to private manufacturers. The positive work in this regard of Universities Allied for Essential Medicines (UAEM) was mentioned.
- *The promise of technology hubs.* One ambition would be to create a permanent hub to develop new, adapted and affordable vaccines such as for HPV. The complexity of vaccine tech transfer can vary from vaccine to vaccine, as well as between developing country vaccine manufacturers. A comprehensive tech transfer from bench to full scale would accelerate development of new products but will need investment and a strong technical platform.

Lessons learnt from cholera vaccine development

Presentation by Rodney Carbis, International Vaccine Institute (IVI)

- Technology was transferred to Shantha Biotechnics in India, with training at IVI, and support in scaling up at the manufacturer's capacity. Clinical trials, including a Phase III trial on

65,000 people in India proved that the vaccine was safe and provides 70% protection. The vaccine was licensed in India in February 2009.

- Lessons learnt: scale up and achieving GMP always presents challenges; what works in the lab does not necessarily work in production; the approval to conduct trials usually takes longer than planned and trials can be further delayed by unplanned events; the terms of the agreement with all parties involved have to be negotiated at the beginning of each project.

Discussion:

- *Determining a market demand.* When you transfer technology there is an assumption from the companies that there is a market - what is needed to show that there is demand? IVI is working on demand forecasts which will help Shantha with their production planning. Since Shantha was bought by Sanofi questions were raised by participants about the potential risk that the oral cholera vaccine will not be marketed by Sanofi because of low demand and lack of profitability of this market. IVI has been assured that Sanofi is committed to manufacture the cholera vaccine and make it available to the public sector at an affordable price.
- *Speed of development.* Does the lack of political prioritisation due to political barriers and disease under-reporting contribute to the lengthy development times for e.g. cholera vaccines versus H1N1? There are issues with introduction of Cholera vaccine with reference to political prioritization and disease under reporting, however IVI is attempting to alter awareness of the problem and have the vaccine introduced in populations where cholera is a particular problem such as West Bengal (India) and Bangladesh. Once the vaccine is WHO prequalified IVI will then start looking at countries in Africa.

Benefit sharing, IP and technology transfer – the influenza virus

Presentation by Sangeeta Shashikant, Third World Network (TWN)

- During the 2007 World Health Assembly, a resolution passed linking virus sample sharing to benefit sharing.
- In December 2008 the Pandemic Influenza Preparedness Framework committed WHO to continue to work closely with Member States and influenza vaccine manufacturers to increase vaccine supply, including strategies to build new production facilities in developing and/or industrialised countries and through transfer of technology, skills and know-how.
- Influenza vaccine manufacturers who receive biological materials as part of the Pandemic Influenza Preparedness framework may grant, subject to any existing licensing restrictions, on mutually agreed terms, a non-exclusive, royalty-free licence to any influenza vaccine manufacturer from a developing country.

Discussion:

- *Can this model be applied to other viruses?* Benefit sharing agreements can be reproduced when countries share viruses with a company. In the agricultural sector for instance benefit sharing is common. The implications of benefit sharing should also be explored in the case of clinical trials e.g. GlaxoSmithKline malaria vaccine trials involve the testing of adjuvants that will be used also for other products; what does this mean for benefit sharing agreements??
- *The investments made in H1N1 may provide an example to follow.* The aim is to get some of the benefits coming back to the shared system. WHO should replicate the work it has been doing with emerging manufacturers in terms of intellectual property (IP), know-how and financial support on H1N1, to other vaccines.

Roundtable IV

New strategies and next steps

Sustainable funding & innovative mechanisms to stimulate needs-based R&D,

Presentation by Laurent Gadot, MSF

- There is a need to move towards a more needs-driven system where innovation and access are envisioned together.
- The right combination of mechanisms to incentivise and fund R&D should aim to ensure that questions of access and medical needs are properly taken into account from the beginning of the process:
 - Pull funding could be appropriate for early stage R&D, as it would allow price/access issues and patients needs to be central to the R&D effort, while at the same time pull funding does not narrow the scope of potential research or participating innovators;
 - This would be facilitated by R&D technical and coordination platform per disease, including IP and tech transfer
 - Push funding for late stage R&D and corresponding manufacturing capacity would allow projects to be carried out by actors without up-front capital
 - Long term purchase commitments. Issues that would need to be addressed include: the capacity to increase competition through tech transfer; the need for profits to correspond to industrial performance, i.e. purchasers would need to agree to a price high enough to interest several producers; the risk of delay between clinical trials and building up of production capacity.

Discussion:

- *Need for early negotiation of access conditions.* These must be negotiated early in the R&D process.
- *How to stimulate needs-based R&D.* There has been funding for initial development of a measles vaccine reliant on heat-stable technology, and an idea to develop a vaccine for children under 6 months which can be incorporated into other EPI vaccines, enabling more routine coverage and that could be developed through technologies that were needle free. But owing to the lack of commercial interest, no further funding has emerged to take the developed technology forward into product development. How can this be addressed? A prize fund, for example, could be a possible incentive.

Meeting Conclusions

Access to newer vaccines:

- Lessons learnt in the past decade with attempts to introduce new vaccines in developing countries:
 - The impact of competition to achieve price reductions, although very effective for EPI vaccines, has not yet been realised for the newest vaccines.
 - Experiences with tiered pricing have so far been mixed and have not led yet to sustainable prices whether in low- or in middle-income countries, particular for new vaccines.
 - Predictable demand alone is not leading to sufficiently reduced prices.

- The price of vaccines has in the past been a neglected question, owing to an assumption that the donor community would foot the bill for rising costs.
- Implications on the GAVI model:
 - Price reductions on newer vaccines such as PENTA, pneumococcal and rotavirus have been disappointing. There is an urgent need to try new strategies to bring down prices.
 - The combination of high prices for newer vaccines and the dramatic downturn in funding commitments partly caused by the global economic slowdown means that GAVI is today facing a dramatic funding shortfall.
 - Given the price of the newer vaccines the current country co-financing only represents a small fraction of total vaccine costs.
 - GAVI's current co-payment mechanism fails to create a market for more affordable vaccines: The country co-pay is the same for the most expensive and complex vaccine as for a cheaper but still adopted one. This is an aspect of the current model that needs to be revisited.
 - Without significant change, the current system is not sustainable.
- Setting priorities for vaccine funding and introduction is a major question today:
 - GAVI's financing shortfall is forcing a new prioritisation process.
 - Upcoming decisions on priority setting will raise difficult governance issues on who will decide; developing countries themselves should have an important say.
 - Decisions should also be guided by a list of "essential vaccines". It will not be defendable to introduce new vaccines and leave, for example, measles insufficiently funded.
 - Prioritisation at the global level will have to leave room for countries to make their own decisions based on local epidemiology fed by adequate surveillance.

Development and manufacture of adapted and affordable vaccines

- The current, market-based R&D system fails to address the need for improved, cheaper and more suitable versions of existing vaccines:
 - Examples include rotavirus and pneumococcal vaccines, and more generally heat-stable vaccine technologies.
 - Nor has GAVI addressed this gap
- There is currently an opportunity to expand R&D and manufacturing capacity in developing countries. However, a number of mergers and acquisitions have taken place that raise the question for how long developing country manufacturers will remain independent from traditional manufacturers.
- Greater investment into not-for-profit R&D is needed to meet the needs of developing countries.
 - The success of the PATH/WHO partnership model in Men A could be replicated.
 - WHO's role is important because of its legitimacy in priority setting
 - GAVI's new strategy, currently undergoing redefinition, includes measures to encourage competition, better leverage price reductions, and support development of new or adaptation of existing products. Greater engagement of GAVI in this area will be needed to achieve its mission and for its own survival. It was however recognized that GAVI cannot become a core player in vaccine development.
 - The creation of a new R&D entity needs careful analysis of pros and cons.

- Technology and know-how transfer is key to shortening the time needed for competitive products to reach the market.
 - A number of technology transfers of developing country-relevant vaccines have been performed successfully. The traditional thinking that transfer of technology must be a down stream approach, starting with fill/finish has not proven to be true – the case studies presented do not support that other models are not viable. The traditional approach tends to transfer a piece of non-critical know-how technology only.
 - The technology transfer hub approach which uses technology and training platforms as an alternative to individual provider–recipient relationships has been used successfully in the context of the influenza vaccine. The technology transfer hub is a key concept that could be replicated for additional vaccines and taken to greater scale. The different technical and financial challenges for each vaccine would need to be considered.
 - Publicly-owned or funded institutes provide an ideal base for a technology transfer hub. EU-based vaccinology institutions could collaborate in such an effort. Yet recent trends appear to be making this collaboration less likely, as evidenced by the decision by the Dutch government to privatize the Netherlands Vaccine Institute.
 - When investing in technology transfer, intellectual property should be dealt with simultaneously.
- IP needs addressing. Additional efforts to analyse, prevent or remove patent barriers are needed, including open licensing policies on the parts of universities and government research bodies and the use of TRIPS flexibilities when appropriate.
- Regulatory requirements, for example through the WHO prequalification are one of the mechanisms to ensure that vaccines meet needs of developing countries in terms of presentations and serotypes.
- Funding mechanisms for R&D should include both push and pull approaches, provide long-term predictable support and aim to ensure affordable products.