One non-traditional approach to immunization financing is Advanced Market Commitments (AMCs.) The essence of the AMC mechanism is an agreement made by donors to guarantee a pre-set fixed price for a fixed market size (number of doses) that will be paid for a vaccine that meets a specific pre-established "target product profile"; this guarantee is made with the understanding that the recipient (developing) countries agree to make co-payments to purchase the vaccine.

Once the commitment is exhausted, manufacturers, having benefited from the subsidy, are contractually obliged either to continue to sell to developing countries at a price that the countries can accommodate over the long term or to license their technology to other manufacturers.

Three major roles were identified for WHO: (i) to provide recommendations on target product profiles through SAGE; (ii) to conduct the prequalification process for AMC-eligible products to be purchased through United Nations agencies; and (iii) to provide technical advice on evidence-based decision-making, priority setting, the introduction of new vaccines, and health-system financing to governments of AMC-eligible countries. SAGE recommends that WHO assumes these functions.

During discussion, it was recommended that the target product profile include elements aimed at reducing systems costs (especially related to the cold chain), such as specifying the presentation and vial size.

SAGE endorsed the role that is proposed for it - that is, to review WHO’s proposals for the target product profile and to make a recommendation on the most appropriate profile.

SAGE recommends that the GAVI Alliance’s secretariat, the World Bank and the AMC independent advisory committee further refine and clarify the AMC’s operating mechanisms so that potential obstacles to effective implementation are addressed.

SAGE recommends that more in-depth investigation should be done of the investments in immunization systems required to support the introduction of pneumococcal vaccine in AMC-eligible countries (which are also GAVI-eligible countries). SAGE also recommends that the impact of different copayment scenarios on the immunization financing profiles of AMC-eligible countries should be further modelled and investigated using more accurate estimates of future demands from countries.
SAGE Recommendations to WHO

SAGE suggested that the GIVS research agenda be expanded beyond clinical trials to include other areas of research, such as health systems research, acceptability and community preparedness studies, epidemiological studies and cost-effectiveness studies.

SAGE praised the overall GIVS costing model and encouraged its further refinement and completion by WHO. Specifically, it was noted that the costing of surveillance and monitoring and for advocacy and communication may have been underestimated.

SAGE requested that the WHO position paper on mumps vaccines be revised, drawing on the conclusions and recommendations from the recent consultation on use of mumps vaccine in the Eastern Mediterranean Region. The revision should take into consideration the accumulating global experience that high coverage with 2 doses of measles–mumps–rubella vaccine (MMR) is required to effectively prevent mumps outbreaks.

SAGE considered that the GIVS goal of 90% (measles) mortality reduction by 2010 remained appropriate. SAGE recommended that work be undertaken to prepare for discussions on the feasibility of a global elimination goal.
SAGE Recommendations to WHO

SAGE Recommendations: (Improving access to quality immunization services in Africa: Challenges and ways forward)
• WHO should advocate globally to assure the additional resources required to fully implement and sustain the RED (reaching every district) strategy so as to ensure a stable transition from the polio infrastructure to a more integrated immunization and child health infrastructure.
• The RED strategy should be integrated into national plans of action for immunization, with especial emphasis on implementation and expansion in lowperforming countries.
• The WHO Regional Office for Africa should rigorously monitor the progress of the RED strategy implementation in each target country in the region, giving the required support to solve problems and document needs.

SAGE Recommendations: (Financial sustainability planning: update on the process)
• WHO and UNICEF should work with all partners to craft an advocacy strategy for fund-raising that makes the investment case for immunization, obtaining political commitment within each country, as well as developing strategies for financing.
• WHO should continue to help improve countries’ ability to plan financially for immunization; increase the predictability of international funds for immunization by working with partners on new financing options and sources such as debt relief, GAVI, IFFIm, and carrying out analytical work on immunization financing through the immunization financing database; and help improve national decision-making and ownership, as well as capacity in financial management.

To support continued success (with measles mortality reduction) WHO must: strengthen routine immunization, assure country ownership of the activities with financial sustainability, and work on integration of measles mortality reduction with other priority health interventions.
It is WHO policy to recommend routine infant HepB immunization as the most effective strategy in countries where the prevalence of chronic HBV infection is 2% or more. In countries with a lower prevalence the immunization of adolescents may be considered as an addition or alternative to infant immunization. However, new information is available which may support a recommendation for routine infant vaccination as the preferred strategy in all countries. SAGE recommends that WHO collect the information necessary to develop a position on universal infant immunization for consideration by SAGE in 2002.

(Regarding OPV cessation, SAGE members) stressed that it was essential for WHO to ensure that countries did not make premature or epidemiologically inappropriate policy decisions before the information generated by research was available.

SAGE recommends that WHO support better coordination between national focal points for nutrition and immunization, including plans that define areas of responsibility for implementation and monitoring.

WHO should ensure that there is unrestricted sharing of samples and vaccine strains internationally.
SAGE Recommendations to WHO

SAGE supported the efforts of WHO to scale up activities relating to influenza pandemic vaccine development, evaluation and capacity building, and the monitoring of seasonal influenza vaccine supply and uptake.

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

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SAGE Recommendations: Synchronous cessation of oral poliovirus vaccine (OPV) use after Global Polio Eradication

• WHO should continue to work with manufacturers and national regulatory authorities to accelerate access to monovalent strains of OPV for use in the vaccine stockpile needed prior to OPV cessation.
• WHO should work with partners to establish a mechanism for rapidly evaluating the candidate IPV that have been developed using Sabin strains (i.e. S-IPV) and, if appropriate, ensure the capacity to transfer such technology, particularly to new manufacturers of IPV.
• To facilitate national decision-making on long-term immunization policy, WHO should, by the end of 2005, develop explicit guidance for OPV-using countries on the impact of IPV on "post-OPV" risks and the implications of IPV use from the financial, programmatic and opportunity perspectives.


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SAGE Recommendations (Intellectual property rights and vaccines):

• To facilitate developing countries’ access to new inventions, WHO should clearly articulate the responsibilities of both private and public-sector intellectual property owners to consider developing-country needs in the management of their intellectual property.
• WHO should continue to take an active role in collecting and analysing information on how intellectual property rights may affect access to vaccines and vaccine development, with the Commission on Intellectual Property and Public Health, to ensure that these issues are reflected in the Commission’s report to be submitted in February 2006.
• WHO should be proactive in helping to resolve the issue of intellectual property rights over reverse genetics for influenza vaccine and generally encourage dialogue and partnership to resolve intellectual property issues for most-needed vaccines, with emphasis on the public health concerns.

**Vaccine Quality**

Additional information on the safety of different mumps vaccine strains is available from country experiences with use of mumps vaccine in mass campaigns and routine settings. These data should be reviewed by the GACVS and the resulting conclusions included in the revision of the WHO mumps position paper.

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

The WHO secretariat should make special efforts to collaborate with industry to increase global availability of MMR vaccines that contain strains of mumps vaccines with the best safety profile.

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

In circumstances where approval for a vaccine was withdrawn due to a failure of an NRA function, the vaccine might be of good quality but not overseen by a functional NRA. If there were no alternative sources of approved vaccine, then SAGE encouraged and approved that WHO facilitate alternative regulatory mechanisms in order to continue to use the available vaccine.

SAGE recommends that in emergency situations where vaccine shortages may compromise immunization efforts a process be implemented that enables WHO staff to obtain appropriate regulatory support; and SAGE requests that these instances be reported to SAGE.


Based on WHO’s review, SAGE confirmed that the benefits of using thiomersal as a preservative in vaccines far outweighed any unproved risks. It was agreed that WHO would uphold a strong advocacy position for the continued use of thiomersal in existing vaccines.

Schedule

The ACPE (Advisory Committee on Polio Eradication) recommended that the risk of importation from polio-infected areas should be reduced further by ensuring all travellers from such areas are immunized, regardless of their age or immunization status; it proposed that a standing recommendation be established to this effect under the International Health Regulations (IHR) (2005).

Outbreak Control

The ACPE (Advisory Committee on Polio Eradication) recommended that the risk of importation from polio-infected areas should be reduced further by ensuring all travellers from such areas are immunized, regardless of their age or immunization status; it proposed that a standing recommendation be established to this effect under the International Health Regulations (IHR) (2005).
SAGE Recommendations to WHO

SAGE requested an urgent expert consultation to review all data on the immunogenicity of fractional doses (of meningococcal vaccine.)

SAGE recognizes the imminent threat of epidemic meningitis in the African Region and the serious shortage of vaccine should this scenario unfold. SAGE concluded that in the event of an epidemic and in the context of vaccine shortage, the national authorities of affected countries should undertake a risk-benefit analysis that recognizes the public health benefits of using fractional doses of licensed polyvalent polysaccharide vaccines during mass vaccination campaigns in order to provide protection to a larger proportion of the population. Limiting vaccination to narrower age groups at highest risk (that is, up to the age of 15 years instead of up to age 29) should also be considered.

SAGE recommended that WHO should provide support to developing countries for the development of national, seasonal and pandemic influenza vaccination policies. All countries should develop pandemic preparedness plans that include strategies for the deployment of vaccines when these become available. SAGE stressed that countries must not depend solely on vaccines for pandemic control because lack of vaccine or at best shortage will be a reality in most countries. With the goal of facilitating equitable and timely access, WHO should continue to play a role in advising on priority groups for immunization with pandemic vaccine (http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_RMD_2004_8/en/index.html).

WHO should provide advice for enhanced surveillance for early detection of new influenza strains and of the onset of a pandemic, if it occurs. WHO should pursue its efforts in strengthening the capability in developing countries of health ministries and national regulatory authorities to facilitate the movement of samples and to ensure prompt registration of pandemic vaccines. Global regulatory convergence should be considered, and WHO should facilitate progress in this direction. WHO should support research and development for pandemic and seasonal vaccines, including alternative and more effective methods of vaccine delivery such as intradermal and intranasal vaccination, improved vaccines and novel production technologies. SAGE noted that there is currently no influenza vaccine production capacity in the African region. Where appropriate, WHO should facilitate developing countries in establishing local capacity for production of influenza vaccine (including pandemic vaccine) based on manufacturers of vaccines of assured quality and should provide support for relevant technology transfer.

WHO should collaborate with expert groups to model the impact of different vaccination strategies in pandemic control, including the possibility of strategic deployment of vaccines, under various epidemiological settings. The risks and benefits of diverting some current vaccine production facilities to the production of influenza vaccines should be investigated. This should be taken forward urgently by WHO as it may provide a means of expanding vaccine production capacity more effectively than reliance on increasing use of seasonal influenza vaccination. The possible negative impacts on supplies of other vaccines should be considered. WHO should ensure that the expertise in rapid mobilization for mass immunization is included in influenza preparedness planning. In addition, similar considerations should be given to access and distribution of antiviral medication.
The global framework (on immunization monitoring and surveillance) describes 2 strategic areas: surveillance for vaccine-preventable diseases and immunization monitoring. The ancillary function of funding surveillance and monitoring is added as a third section.

The vision of the global framework is that, by 2010, there should be an integrated epidemiological, laboratory and programme-monitoring network for the surveillance of vaccine-preventable diseases and monitoring of the performance of immunization programmes. This network will provide high quality information to measure the impact of vaccination and maximize the safe, effective and equitable use of vaccines at country, regional and global levels to reduce or eliminate the burden of vaccine-preventable diseases.

SAGE endorse the global framework documents with some modifications. Modifications suggested included: expanding the linkages to the IHR (International Health Regulations) by providing examples of how some vaccine-preventable diseases fit into the new IHR because they constitute a public health emergency of international health concern; including operational guidance on ways to implement this strategy at the local level in the “Way forward” section; defining key epidemiological data used in the furtherance of mathematical modelling; and emphasizing recent developments on surveys to monitor programmes and to validate estimates (for example, it is now recommended that Multiple Indicator Cluster Surveys take place every 3 years instead of every 5 years).

SAGE suggests that WHO should produce a clear dissemination plan for the global framework.

WHO should particularly strive to obtain more data on the epidemiology of meningococcal serogroup in Nigeria where currently no laboratory data are being collected by the African network.
SAGE Recommendations to WHO

**Research**

SAGE recognized the importance of activities targeting capacity building and the development of clinical trial sites to ensure that all phases of clinical trials could be conducted in a way that meets the highest scientific, legal, ethical and regulatory standards as well as ensuring that communities are involved in the process. It will be important to develop such sites in developing countries where future vaccines would offer the most benefit.

Recognizing the complex scientific questions that need to be addressed with novel vaccine technologies, SAGE encourages efforts to facilitate close interaction and early discussions between researchers and national regulatory authorities. Additional training of members of national regulatory authorities in scientific aspects should also be included in the training programmes that are being implemented by WHO and other international sponsors.

SAGE expressed its support for the work of WHO in the area of developing vaccines against HIV, TB and malaria in close cooperation with other international and national partners and confirmed the critical role WHO has in developing relevant policies, norms and standards to facilitate the highest scientific, regulatory and ethical standards of clinical trials worldwide.

Conclusions and recommendations from the meeting of the immunization Strategic Advisory Group of Experts (SAGE) - November 2006


**Database ID**  89_21  
**Year**  2007

SAGE recognized the critical role that WHO should play in the international coordination of research and evaluation of influenza pandemic vaccines.

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

Weekly Epid. Record (2006, 81: 210-20)  

**Database ID**  82_17  
**Year**  2006

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Introduction of Vaccines

SAGE recommended that WHO gives a clear signal on the priority for wider use of pneumococcal vaccine in children.

Lack of clarity of demand is a critical factor inhibiting industrial scaling up of manufacturing capacity. This uncertainty needs to be overcome since validated demand forecasts are essential for the commitments required from industry that will make this vaccine available at affordable prices.

In particular, evidence was required through studies on disease burden of the cost benefit of using pneumococcal conjugate vaccines and the feasibility of vaccine delivery to all vulnerable groups.

Pneumococcal serotype prevalence studies, undertaken in different settings, are required to judge the appropriateness of the conjugate vaccine to be used. A firm position from SAGE will be required once serotype prevalence studies are completed to judge the appropriateness of the conjugate vaccine available.

(SAGE) recognized that a global recommendation, made before resolution of funding and supply issues, could leave vulnerabilities that have been experienced with the implementation of Hib vaccine.

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 9-11 November 2005

SAGE Recommendations: Synchronous cessation of oral poliovirus vaccine (OPV) use after Global Polio Eradication

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