A New Access Paradigm: Public Sector Actions to Assure Swift, Global Access to AIDS Vaccines

International AIDS Vaccine Initiative
IAVI Access Project White Paper
June 2001

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Executive summary

For the first time since the global AIDS epidemic began, the world is seriously debating how best to respond to this unprecedented health crisis. Behavioral prevention programs must be expanded and individuals living with HIV infection should have access to effective treatment and care. Concerted action must address the many barriers that inhibit the availability and effectiveness of these interventions.

Yet safe and effective vaccines are the most practical and sustainable means of reducing the massive suffering, mortality, and economic burdens caused by the global AIDS epidemic. Consequently, any comprehensive initiative against HIV/AIDS must include effective interventions to speed the development and delivery of AIDS vaccines.

A strategy to ensure timely availability of AIDS vaccines includes a series of initiatives involving research, regulation, production, purchase, and distribution. A pick-and-choose approach that ignores any of these key issues is certain to mean substantial delays in the availability of and/or reduced access to such vaccines.

If the public sector does not take quick, decisive action, swift global access to AIDS vaccines will not occur

Why action is needed now to ensure access to AIDS vaccines

If the public sector does not take quick, decisive action, swift global access to AIDS vaccines will not occur. Existing access paradigms—both in vaccine and AIDS drug development—clearly demonstrate the consequences of waiting for product licensing before addressing critical access issues.

Today, developing countries must still wait an average of 20 years after new vaccines are licensed in industrialized countries before they are introduced to their own populations. This unacceptable delay stems from numerous factors, including the absence of mechanisms and funds to purchase vaccines, the slow pace at which companies scale-up worldwide manufacturing capacity, needlessly long regulatory hurdles, and the lack of effective systems to distribute new vaccines in resource-poor countries. The Global Alliance for Vaccines and Immunizations (GAVI) is working to change this paradigm. These efforts must be supported. But without radical changes in the way vaccines are developed and distributed, this deplorable process is certain to be repeated when AIDS vaccines are introduced.

Similarly, the lack of access to effective anti-retroviral therapy in developing countries, long after such drugs were introduced in industrialized countries, also demonstrates the utter failure in waiting until effective products are licensed before addressing access issues.

In short, access to AIDS vaccines is not tomorrow's problem. Waiting to address access issues until after AIDS vaccines are licensed will sentence millions to preventable illness and death.

Specific actions that the public sector needs to take

Actions that the public sector can take now to ensure access to AIDS vaccines include the following:

1 **Create financial mechanisms—an account or "window" within a broader Global Health Fund[1]—to support the purchase and delivery of HIV vaccines**

One critical component to a global access strategy for AIDS vaccines is the creation of credible financing mechanisms to support the purchase and delivery of such vaccines. Earmarked financing for AIDS vaccine purchase is essential. An AIDS vaccination account should be created, and credible commitments to finance it once AIDS vaccines are available should be made.

Developing countries must still wait an average of 20 years after new vaccines are licensed in industrialized countries before they are introduced to their own populations

This Fund or account (although not necessarily the financing for it) should be put in place well in advance of an actual vaccine to permit effective planning by governments and to spur private sector investment in vaccine research, development, and production. The Fund could be linked to other financing to allow countries to select their preferred option—direct grants from the Fund, leveraged grants, or combined loans and grants. The leveraged grant alternative may be particularly advantageous for low-income countries, as it would allow them to substantially increase financing from the Fund by a factor of three without any repayment obligations.[2]

In creating a global health or AIDS vaccine fund, the following criteria should be included:

- Sufficient funding.
- Broad support and representation from both financial donors and developing countries.
- Support for both commodities and delivery systems.
- Availability to all developing countries.

[1] Inclusion of a separate sub-account for AIDS vaccination within a larger health fund is the ideal, but should this not be possible, an AIDS Vaccination Fund could be a stand-alone fund.

[2] Leveraged grants involve using grant financing to pay off all (or some) debt so that little or no actual debt is incurred by the recipient. For low-income countries, the factor of three multiplier is calculated using an estimated concessional element of World Bank International Development Agency (IDA) credits of 66 percent.

- Financing should be "new" money clearly allocated to AIDS vaccines, not funds transferred from treatment[3] or other health needs.
- Financing should primarily be in the form of grants, although loans can be used to complement these. Countries should have the right to choose the financing instruments.
- Financing for vaccination must be sustainable over a number of years.
- Funding mechanisms should be linked to avoid duplication; minimize transaction costs; and ensure rapid application, approval, and disbursal processes.
- Funding decisions should be based on clearly specified criteria that are fairly applied.

2 **Support tiered pricing**

Tiered, or differential, pricing permits developing countries to receive favorable prices, but it requires that the global public sector support appropriate market segmentation and that commercial firms receive a reasonable return on their investment in industrialized countries.

3 **Support aggregated procurement for developing countries**

Bulk purchasing or joint negotiation mechanisms should be available to all developing countries.

Credible financing mechanisms to support the purchase and delivery of AIDS vaccines are essential

4 **Increase support for accelerated AIDS vaccine research and development, while creating real incentives for private sector investment**

Greater public sector support for AIDS vaccine development is desperately needed. To meaningfully accelerate product development efforts, particularly those focused on creating products appropriate for developing countries, at minimum, another US$ 1.1 billion will be needed over the next seven years. Financial and technical support should be provided for clinical trial testing, with particular attention to the need to build capacity in developing countries to host efficacy trials. Where public funds are used to support vaccine-related research and product development, grant agreements should include, where possible, provisions that promote access for developing countries (i.e., through pricing and supply strategies or through the sharing of intellectual property). Greater efforts must be made to spur private sector investment in AIDS vaccine development. Providing meaningful tax benefits for companies investing in AIDS vaccine research can contribute to the rapid development of effective vaccines.

[3] The long-term nature of the infection implies that those already living with HIV/AIDS will require effective care and treatment for many years after an effective AIDS vaccine becomes available.

5 **Promote regulatory reform and coordination to ensure that AIDS vaccine trials and product licensing are not burdened by unnecessary delays**

Regulatory agencies should rapidly seek agreement on key scientific matters necessary for clinical trial and product licensing approval. They should also streamline and coordinate dossier requirements and submission processes, and develop fast-track approval processes (no longer than six months) for life-saving products. Countries with similar epidemiological and population characteristics could benefit by pooling their regulatory expertise and linking approval processes.

6 **Work with private industry to ensure sufficient and timely supply of AIDS vaccines to meet global needs**

Because a number of factors may limit the private sector's ability or willingness to install the production capacity required to rapidly meet developing country needs, the public sector must be ready to establish innovative mechanisms to ensure that supply does not become an access barrier.

Equitable access to AIDS vaccines requires the creation of a new paradigm characterized by a proactive view, novel interventions covering a range of areas, and new, as well as expanded, collaborations

Equitable access to AIDS vaccines requires the creation of a new paradigm that is characterized by a proactive view, novel interventions covering a range of areas, and new, as well as expanded, collaborations. This paper offers specific technical recommendations for establishing this paradigm for AIDS vaccines. Translating these into action and results will be challenging, but is feasible. What have been missing and are required from the global public sector are the key ingredients that no document can provide—political will and courage.

1 Introduction

Each minute, at least ten new people are infected with HIV. Already, over 34 million people are living with HIV/AIDS—more than 90 percent of these in developing countries. The world urgently requires an effective response to this pandemic.

Growing concern over global disparities in access to treatments, combined with a dramatic lowering of prices for anti-HIV drugs, have prompted international leaders to consider new financing options to address HIV/AIDS. Advances in the treatment of individuals with HIV/AIDS are essential, but these interventions should complement, not replace, effective prevention.

Efforts to improve prevention and expand the range of preventive options continue to be of vital importance. A vaccine is likely to represent the most practical, effective, and sustainable means of controlling HIV/AIDS. Hence, its rapid development and widespread use must be promoted in any comprehensive initiative.

Involvement by the public sector[4] is essential. Preventive AIDS vaccines are global public health goods. While they stand to provide private benefits to the individuals receiving them, they also bring larger societal benefits through reduced transmission, eventually reduced treatment costs, and enhanced economic productivity.

Involvement by the public sector is essential, as preventive AIDS vaccines are global public health goods

Moreover, the private sector has been slow to invest its own resources in AIDS vaccine development, due primarily to the significant scientific challenges and because the greatest need for such products are in countries that can least afford them. Therefore, the public sector must take a leading role in driving solutions and in creating an environment in which civil society and the commercial private sector can also contribute to improve access.

Access requires more than adequate financing and reasonable prices; it is determined by a multiplicity of factors. Because of this, widespread, timely, and appropriate use of an AIDS vaccine will only happen if policymakers pursue a package of coordinated public sector actions.

[4] Throughout this document, "public sector" refers to governments of developing and industrialized countries as well as multilateral institutions, such as the United Nations, its specialized agencies, and the World Bank Group.

Consider the typical trajectory for deployment of a vaccine:

- concept development;
- pre-clinical testing in animals, to assess immunogenicity, safety, and other characteristics;
- clinical testing in humans, first to test safety and basic product attributes, and later to determine efficacy;
- production, for which installing industrial capacity can require four to five years and more than US$ 100 million;
- regulatory assessment; and
- "access interventions" involving the development of policies for use, the mobilization of resources for product purchase and delivery, the establishment of purchase mechanisms, and the creation and maintenance of delivery infrastructure.

This sequential approach to development and delivery of essential global public health goods necessarily consumes a substantial amount of time. Typically, one-half or more of the people in developing countries who could benefit from a vaccine do not have appropriate access 20 years or more after initial licensure. (Annex 2 presents more details of a typical timeline for vaccine product development and access.)

The immense challenges in providing access to AIDS treatments in developing countries demonstrate the need to begin planning as early as possible

In addition, the immense challenges in providing access to AIDS treatments in developing countries demonstrate the need to begin planning as early as possible.

Alternatives to these paradigms are possible. However, because so many different steps are inextricably linked with others, only coordinated action will remove access barriers and create incentives to ensure swift distribution in developing countries of new AIDS vaccines. In particular, the "access interventions" traditionally left for last (or not attended to at all) must be addressed earlier and dealt with aggressively.

This paper outlines specific public sector actions in five key areas—financing, pricing, regulatory processes, research and development, and production capacity. If these actions are pursued, widespread access to AIDS vaccines can be achieved in at least half the time than has typically been required for other vaccines. (The new timeline that would result from such coordinated action is outlined in Annex 3.) This result is not only desirable, it is entirely feasible—but only if the global public sector takes aggressive and coordinated action now.

2 Financing AIDS vaccine purchase and delivery

Establishing credible financing to purchase and deliver AIDS vaccines is central, though not by itself sufficient, to ensuring access to such vaccines. While the existing access paradigm would wait to address this issue until a vaccine is available, that approach will not yield the desired result of rapid, widespread access.

2.1 Creating financing mechanisms in advance of vaccine availability

Advance creation of financing mechanisms for vaccine purchase and delivery is essential for several reasons:

- *Incentives for commercial research and development* Substantial, credible financing creates a market for new products in developing countries that otherwise would not exist and can drive commercial producers to invest in research and development. The assurance of such financing now would spur increased industry investment in vaccine R&D.
- *Country planning and introduction strategies* With the knowledge that financing will be available, developing countries can plan vaccination introduction and delivery strategies prior to product availability, so as to ensure rapid and appropriate adoption. Advance consideration of policy issues can permit certain policy questions to be addressed in the clinical trial phase, thereby speeding product introduction even further.
- *Production capacity* A credible market demand in developing countries and the ability of these countries to better specify their needs in advance of vaccine availability will contribute significantly to efforts to ensure that adequate production capacity is put into place (plants for large-scale production must be started four to five years prior to planned licensure).

Substantial, credible financing creates a market for new products in developing countries that otherwise would not exist and can drive commercial producers to invest in research and development

This does not imply that AIDS vaccines should compete with existing products for funding today. What is essential is the establishment of a funding mechanism (which, in an expanded form, may also be relevant for other health products) that is credible (all parties believe that promised monies will become available) and through which appropriate funding for AIDS vaccines can flow when it is needed.

2.2 Key requirements for an AIDS vaccine fund

Any financing architecture for preventive AIDS vaccines should adhere to the following criteria:

- *Broad support from and representation by financial donors and developing countries* Such support and governance is essential to ensure that the financing meets the real needs of developing countries. The system must be one that the donor community has enough confidence to invest in.

- *Support for both commodities and delivery systems* A vaccine must be appropriately used, not just purchased. Delivering AIDS vaccines will require substantial investment in infrastructure to reach intended populations. The childhood vaccine delivery systems (which are themselves underdeveloped in some countries) can be used to only a limited extent because AIDS vaccines are unlikely to be utilized in children at first.[5] Moreover, since AIDS vaccines will initially need to be introduced to adolescents and adults at high-risk for HIV infection (particularly injection drug users, commercial sex workers, and others), new mechanisms for delivering the vaccines will need to be created. Development of a meaningful infrastructure will require strengthening of the health sector as well as providing appropriate education to care providers, vaccine recipients, and the population as a whole. Additionally, the proper balance between purchase financing and delivery financing will differ according to the vaccine's features. Utilization of partially effective vaccines may require sustained investment in other prevention measures, including behavioral modification strategies.

AIDS vaccines should not compete with existing products for funding today

- *Availability to all countries* While financing mechanisms should place a priority on the poorest and most afflicted countries, successful new product introductions will require that the financing needs of a broader range of countries be met. Mid-income countries can find it difficult to rapidly mobilize sufficient financing to introduce a vaccine early in its product life (particularly if "catch up" campaigns are deemed desirable). A goal of rapid, widespread global access cannot be achieved by focusing only on the financing needs of the poorest or most afflicted countries.

- *Sufficient levels of financing* Although the exact amount of AIDS vaccine-related financing necessary cannot yet be stipulated,[6] a

[5] This is due to lack of clinical data and it being more cost-effective to target other populations.

[6] The need and demand for AIDS vaccines in developing countries is currently being quantified. Two complementary efforts are underway to address this issue: a joint IAVI-WHO-UNAIDS project and a European Commission-funded World Bank project.

conservative calculation easily places the need in the *billions (not millions) of dollars.*[7]

- *Specificity* This financing must be clearly and specifically identified for AIDS vaccines. It should not compete with funding for AIDS treatment, as a vaccine cannot immediately replace treatment and care (these will be required for many years beyond the availability of an effective vaccine due to the long-term nature of the infection). Indeed, a financing system based on a large "pot of money" shared by many products increases the risk of inadequate financing for all of the products.
- *Suitability of instruments* To ensure that health objectives are met without placing excessive burdens on fragile economies, and to encourage the most rapid introduction of AIDS vaccines possible, the financing must be structured primarily as grants. Loans should be used only to complement these.
- *Sustainability* Vaccination efforts will need to be sustained over a long period of time. Furthermore, it is anticipated that several generations of AIDS vaccines will be introduced and that the population to be immunized will increase as efficacy or ease of administration improves. It is likely that as new vaccines become available, some countries will run "catch up" campaigns covering larger populations prior to shifting to regular vaccination of cohorts. While there will probably be fluctuations in financing needs, on the whole, these are likely to increase for a period of one to two decades after the first vaccine becomes available.
- *Choice of financing systems* Countries have different needs and different preferences. The financing system for AIDS vaccines should not impose one solution upon countries, but rather allow countries to choose what best suits their needs.
- *Incentives for vaccine introduction* Financing should be disbursed in ways that encourage countries to speed introduction of AIDS vaccines. The financing system should be structured in a way, and at a time, such that it provides incentives for private industry to invest in research, development, and production capacity sufficient to meet developing country needs.
- *Efficiency in funding* Linking sources of financing, and providing a single entry point for requests for vaccination financing, will help avoid

A conservative calculation easily places the level of financing needed in the billions—not millions—of dollars

[7] The population of adults in low- and mid-income countries is 3.3 billion. If only 10 percent of this population is vaccinated, and cost is assumed to be US$ 10 for a course of vaccination, then US$ 3.3 billion will be required to pay only for the vaccine. Delivery and costs for other related supplies can easily double this figure. While external assistance cannot be expected to cover all these expenses, it will need to cover a substantial portion for the poorest countries. It follows that any effective financing mechanism must be capable of disbursing billions of dollars annually.

duplication, and minimize transaction costs. Application, approval, disbursal, and review processes should be effective and rapid.

- *Transparency and accountability* Funding decisions should be based on clearly specified mechanisms and criteria that are fairly applied. All parties handling or utilizing funds must agree to independent reviews.

2.3 Existing financing for HIV vaccines

Billions of dollars will be required to assure rapid and widespread access. To put this into perspective, a study jointly undertaken by UNAIDS and the Harvard School of Public Health, found that only US$ 548.5 million was spent in 1996 on AIDS programs in developing countries. For 45 percent of these countries, national resources accounted for less than 10 percent of overall financing.

Although official development assistance (ODA) has grown, the rate of growth has not kept pace with the rapid spread of HIV/AIDS. In 1997, ODA funds per HIV-infected individual were less than half what they were in 1988. Similarly, this same study indicated that in the period between 1986 and 1997, World Bank loans and credits for HIV/AIDS prevention and control amounted to US$ 580 million.[8] In the period from 1996 to 2000, the World Bank committed US$ 493 million to HIV/AIDS project components.[9]

A vaccine must be appropriately used, not just purchased, and so delivering AIDS vaccines will require substantial investment in infrastructure to reach intended populations

For low-income countries, some specific financing mechanisms have already been established for HIV/AIDS or for vaccines. (See Table 1.) Some of these rely upon IDA credits offered by the World Bank on concessional terms.[10] Yet, many countries are understandably reluctant to incur additional debt. This may impact the willingness of such countries to participate in particular financing mechanisms, even to combat HIV/AIDS.

[8] Joint United Nations Programme on HIV/AIDS (UNAIDS). *Level and flow of national and international resources for the response to HIV/AIDS, 1996-1997.* (Geneva: UNAIDS, 1999).

[9] www.worldbank.org/html/extdr/pb/pbaidsactivities.htm (on May 31, 2001)

[10] Countries eligible for International Development Agency (IDA) credits generally have a per capita annual income of US$ 885 or less. Some countries with a higher income (up to US$ 1445) may be able to use IDA credits to finance activities in certain areas only. The typical terms of IDA credits are: 10 year grace period, maturity at 40 years, principal repaid at 2 percent for years 11-20 and at 4 percent for years 21-40.

Table 1 Selected current financing mechanisms for vaccines or HIV/AIDS programs available primarily to low-income developing countries

Name	Purpose	Funded by	Designated for	Amount/Form
Multicountry HIV/AIDS Program for Africa (MAP).	Support for national HIV/AIDS prevention and care programs.	World Bank, UNAIDS, International Partnership Against AIDS in Africa.	Governments of African countries qualifying for IDA credits that have a strategic approach to combat AIDS, an HIV/AIDS coordinating body, and are willing to work through and with communities, civil society, and the private sector.	US$ 500 million in the form of rapid and flexible IDA credits supporting national HIV/AIDS prevention and care programs.
World Bank Commitment to IDA Financing for Communicable Diseases.	Support for national efforts in the prevention and care of tuberculosis, malaria, and HIV/AIDS.	World Bank.	Governments of countries qualifying for IDA credits.	US$ 1 billion in IDA credits, to be replenished as needed.
The Global Fund for Children's Vaccines (GFCV) also known as the GAVI fund.	Financial support for the adoption of new and underused vaccines in childhood immunization programs (procurement providing vaccine in-kind, delivery infrastructure, and possibly R&D).	The Bill & Melinda Gates Foundation and the governments of the Netherlands, Norway, the United Kingdom, and the United States.	Governments of 71 countries with an income <US$ 1000/capita and a population <150 million, meeting certain DTP3 coverage requirements.[11]	US$ 1 billion (over five years).

[11] Special arrangements may be adopted for China, India, and Indonesia.

Although GAVI is not presently structured to handle AIDS vaccine financing, it may be able to do so in the future. This would require, at a minimum, substantially greater funding, a specific account for AIDS vaccines and their delivery, attention to delivery issues related to adolescents and high-risk groups, and an expansion of the number of countries that qualify for GFCV support.

For mid-income countries, the external financing choices are more limited than for the poorest, although many of these countries can apply for IBRD[12] loans from the World Bank.

Under certain conditions, loan financing can be used effectively to improve health, but it also has significant drawbacks. Many poor countries are already heavily indebted and are reluctant to utilize this form of financing. Furthermore, the typical process of prolonged country-by-country negotiations for new loans may not be appropriate for the introduction of AIDS vaccination, where time will be of the essence.

In short, existing financing mechanisms are valuable, but fall considerably short of meeting many of the previously outlined features key to optimal AIDS vaccine financing. Significantly more funding is necessary, but a cohesive framework that specifically addresses AIDS vaccines and can facilitate swift action is also required.

Existing financing mechanisms are valuable, but fall considerably short of meeting many of the features key to optimal AIDS vaccine financing

2.4 Proposed structure for financing AIDS vaccine purchase and delivery

To ensure that funding levels are appropriate and that clear, unambiguous incentives are given to industry, it is proposed that an AIDS Vaccination Fund be created. Such a fund could be linked to, or part of, broader mechanisms, but separate, earmarked financing (or an account) within a larger fund is essential.

Key components of an AIDS Vaccine Fund or broader fund include:

- *Sources of financing* Financing should be broad-based with contributions on a regular (such as annual or biannual) basis made by bilateral agencies, foundations, charities, and corporations and individuals (probably via a designated charity or foundation for tax reasons).
- *Housing* A "housing" arrangement is required for the management of the monies within the Fund as well as the handling of other

[12] International Bank for Reconstruction and Development (IBRD) loans are generally available to countries with per capita incomes less than US$ 5225. The typical terms of IBRD loans are: a 3-5 year grace period, maturity at 15-20 years, market interest rates.

administrative functions. The Fund could be established as a trust fund at the World Bank; managed by another international organization (such as UNAIDS and/or WHO); or treated as an extension of the GAVI Fund. Ideally, an AIDS Vaccination Fund would share overhead costs with other funds.

- *Governance* Regardless of where the Fund is housed, governance should include representatives of both contributors to, and beneficiaries of, the Fund.

- *Policy direction* Health-related UN technical agencies, such as WHO and UNAIDS, would be responsible for establishing appropriate policies to guide countries and financing institutions.

Sub-accounts The Fund could include three sub-accounts focusing on specific activities:

1 *Purchase sub-account* This sub-account would be used by countries for the purchase of vaccines, syringes, safety boxes, and other related recurrent supplies. It should be specific to preventive AIDS vaccines.

2 *Delivery sub-account* This would cover delivery costs that are specific to AIDS vaccination programs such as cold chain supplies and vehicles, training of health workers and educational efforts for recipients and the general public, and fully dedicated staff as well. It can also cover more general costs (shared staff, facility, vehicles) if it is determined that these are not appropriately covered by other methods. If general costs are covered, and if the AIDS Vaccination Fund constitutes a component of a larger fund for health products, the delivery sub-account can be shared across products.

An AIDS Vaccination Fund could be linked to, or part of, broader mechanisms, but separate, earmarked financing is essential

3 *Preparation, Monitoring, and Evaluation (PME) sub-account* This would fund preparation of vaccination projects and proposals as well as subsequent monitoring and evaluation. Financing would flow to the parties carrying out these activities. For example, financing for project preparation and proposal development would be provided to the country and any agencies assisting it.

2.5 Specific mechanisms for financing AIDS vaccine purchase and delivery

Monies to support AIDS vaccination could flow to developing countries in three ways:

1 *Direct grants* This constitutes a direct grant from the fund to the country. In order to ensure rapid introduction of AIDS vaccines in developing countries, a significant amount of resources will be

required. For mid-income countries, financing would be available only for a limited period of time after the licensure of a vaccine in a suitable reference country.[13] Should a different, significantly improved AIDS vaccine become available at a later time, the Fund would permit countries to request additional financing to cover new introduction costs.

2 *Leveraged grant financing (*"de facto" *grants)* Countries would be able to "leverage" grant financing through a matching IDA credit (for low-income countries) or IBRD loan (for mid-income countries). In essence, after a country takes a credit or loan from the World Bank, financing from the Fund would repay what is owed by the country to the Bank in full (for low-income countries) or in part (for mid-income countries). For low-income countries, this leveraging would allow them access to significantly greater financing than would be available under Option 1, but still allow them the advantages of *de facto* "grant" financing (i.e., nothing to pay back). Mid-income countries would also have more money at the start than would be available through Option 1. Although they would be required to repay the loan, terms would be more concessional than usual (the loan would be paid back on interest rates that vary somewhere between IDA and IBRD, depending on the need of a given country). As with Option 1, mid-income countries would only be able to access this financing for a limited period of time.

The countries themselves should select the form of assistance—grants, loans, or a combination

3 *Combination grant and loan financing* Countries would be able combine grant financing from the Fund with loan financing. This option would provide countries the greatest financing at the start of vaccination efforts, although both low-income countries and mid-income countries would be required to repay the loan component under standard IDA terms (for low-income) or IBRD terms (for mid-income countries). As with the other options, mid-income countries would only be able to access financing from the Fund for a limited period of time.

Some countries may prefer to use only grants or *de facto* grants. From a public health perspective, it would be preferable to provide as much funds for direct grants for AIDS vaccination as possible. Yet some countries may prefer to have the maximum amount of funds available at the start to better blunt the epidemic, and thus would be willing to incur some debt. In all cases, it would be the countries themselves that select the option. The amount of financing any given country would receive from the Fund would be the same regardless of the choice.

[13] Industrialized countries, although they are likely to license first, may not be appropriate reference countries given epidemiological differences. It may be preferable to designate regional reference countries.

Countries would be responsible for preparing proposals, but extensive assistance from WHO, UNAIDS, and development banks would be available to countries that request it. This system provides countries with "one-stop financing" for AIDS vaccines in that a single proposal would be used as the application for the Fund (both purchase and delivery sub-accounts) and to the World Bank (if any loan financing is requested).

Proposals would request financing based on a comprehensive plan of action and would also indicate how domestic (and any other) financial resources would be directed.

The Fund and the Bank would adopt coordinated and expedited procedures for reviewing and approving proposals. For the World Bank, this proposed financing scheme necessarily implies a simplification of standard practices leading to expedited review and disbursement.

Proposals should identify desired outcomes and indicators for measuring progress. To continue to receive Fund and World Bank financing, countries would be required to demonstrate a minimum, mutually agreed, acceptable level of progress towards meeting identified outcomes.

National treasuries, bilateral agencies, foundations, and other parties are called on to make nominal contributions now, accompanied by statements committing themselves to significant levels of future support

2.6 Level of financial commitments

For the Fund to yield measurable benefit, it should be able to disburse a significant amount of funds each year (minimum US$ 1 billion[14] annually, but much more may be required). Even while other pressing global health needs may make it difficult for the global community to set aside much of this financing immediately, nonetheless, national treasuries, bilateral agencies, foundations, and other parties are called on to make nominal contributions now (sufficient to establish the Fund and make visible a commitment to it), accompanied by public, written statements committing themselves to specific, significant levels of financial support following the availability of an AIDS vaccine.

It is likely this financing system will place a new range and magnitude of demands on World Bank financing, particularly IDA loans. Hence, there must also be agreement among the governments that contribute to the Bank that resulting increased demands for IDA replenishment will be met.

International meetings such as the United Nations General Assembly Special Session on AIDS (June 2001, New York) and the Meeting of

[14] This figure reflects the purchasing power of dollars today. Over time, it must be adjusted for inflation so that purchasing power does not diminish.

G8 Nations (July 2001, Genoa) provide an ideal opportunity to make firm commitments to fund the delivery of AIDS vaccines to all who need them throughout the world, when such vaccines become available.[15]

3 Pricing

Pricing of AIDS vaccines poses a difficult dilemma. Although meaningful global access will not be achieved if prices are too high, firms will not invest in AIDS vaccines if they cannot achieve a suitable return on their investment. Steps to build a rational approach to pricing must bear this in mind.

Acceptable pricing requires that there be a proper balance between supply and demand. Hence, a key step, discussed in the previous section, is to ensure that credible financing exists. It will also be important to assure that the vaccine supply is sufficient to meet the demand (this is discussed in more detail in section 6).

Governments and multilateral institutions must create an environment that supports pricing levels appropriate to different countries' ability to pay

Like some other global public health goods, AIDS vaccines will likely appeal to both industrialized and developing country markets. Universally low prices are not viable because firms would not be able to achieve sufficient return on investment. Universally high prices limit access to the poor. It follows then, that governments and multilateral institutions must create an environment that supports pricing levels appropriate to different countries' ability to pay (sometimes called tiered pricing).

Tiered pricing is currently used for established children's vaccines and for other selected health products (including condoms and oral contraceptives), and has the support of leading international organizations (including the European Community, the World Health Organization, and Médecins sans Frontières) as well as the pharmaceutical industry. Despite this, support for tiered pricing structures is not entirely uniform, and practical issues regarding its extended implementation remain to be addressed.

[15] IAVI has proposed the following language to be part of the UNGASS Final Declaration: "(Governments participating in the Special Session) agree to commit the necessary resources to provide AIDS vaccines, when they are available, to all who need them without delay."

Tiered pricing does not imply public sector price-setting or additional price regulation; rather, public sector actions should:

- *Build support* Societal acceptance in industrialized countries is required to ensure that firms can obtain reasonable returns and avoid the risk of backlash that can keep them from implementing this pricing structure. This requires, among other things, that the mechanisms to ensure access in these countries be clear and adequate.
- *Segment markets* Industrialized and developing countries must work together to develop reliable means to prevent the importation to industrialized countries of lower-priced vaccines sold to developing countries. All countries must provide credible assurances that they will not allow this. A jointly devised and implemented system to effectively monitor and enforce agreements may be necessary, and participation in such a system can be made a precondition for countries to obtain favorable prices.

Buyers may find themselves at a disadvantage in an AIDS vaccine market with only one or very few producers. To balance supplier power in the market, developing countries should have the option to join together in larger purchasing or negotiating groups, thereby leveraging sizeable volumes to obtain more favorable prices.

Developing countries should have the option to join in larger purchasing or negotiating groups, thereby leveraging sizeable volumes to obtain more favorable prices

Consideration should be given to possible roles for existing vaccine procurement mechanisms, including the Pan American Health Organization (PAHO) Revolving Fund[16] and UNICEF's procurement system (which is also linked to the Vaccine Independence Initiative and now to GAVI/GFCV financing).[17] Although these mechanisms are extremely valuable, not all developing countries have access to them. The creation of new mechanisms that group together countries of similar need and economic situations may be desirable.

[16] The PAHO system purchases childhood vaccines, including those against *Haemophilus influenzae* Type b (Hib) and hepatitis B, for Latin American and Caribbean countries that choose to participate. Under the revolving mechanism, PAHO (in many, but not all, cases) makes advance purchases of vaccines and is repaid by countries in local currency once the vaccine is delivered. Countries participating in the PAHO fund receive technical support in such areas as immunization policy, strategic planning, and delivery logistics.

[17] UNICEF purchases traditional childhood vaccines for developing countries (covering about 65 percent of the world's children). UNICEF's Vaccine Independence Initiative (VII) offers participating countries a short-term credit line to purchase vaccines in local currency, although countries are not required to participate in VII to take advantage of UNICEF's bulk or aggregated purchase service for traditional vaccines. Newer, underused vaccines, such as those for hepatitis B and Hib will be purchased with GAVI/GFCV financing. For these products, bulk procurement services will be offered only to the subset of low-income countries that qualify for GAVI/GFCV financing, which is an approach to market segmentation intended to obtain the lowest effective prices for the poorest countries.

The public sector can also apply "access conditions" (benefiting developing countries) to grants extended to private firms. In effect, the public sector would receive agreements from these firms on access-relevant issues for developing countries (prices, production volumes, technology transfer). The precise terms of such agreements must be negotiated individually between the interested parties.

Additionally, governments of countries with vaccine industries can provide tax relief for appropriate donations. Such incentives should not be seen as substitutes for adequate financing and developing tiered pricing. Yet they can be complementary to these efforts. The United States already provides a donation tax credit with a possible "enhanced" deduction for drugs or vaccines under certain conditions. The United Kingdom is developing a donation tax credit for drugs and vaccines. Ideally, tax incentives for donations would be harmonized across countries so as to maintain balanced competitive conditions among firms.

It is desirable to structure vaccine donation tax relief to reward only donations that:

- are given to countries (directly or through a purchase fund) on a predictable, sustainable basis such that they may be accounted for in country planning and budgeting; or
- are given to respond to acute needs in times of natural disaster or other emergency situations; and
- otherwise meet internationally agreed upon precepts (including being of good quality, possessing an acceptable shelf-life, etc.).

Strong public sector support for basic research and product development is essential

4 Supporting accelerated research and product development

Vaccine development is a long, costly, and risky undertaking. It can take fifteen years or more from origination of the vaccine concept to widespread global licensure of a product. (The process includes basic research, pre-clinical/animal testing, clinical testing, and production scale-up.) In terms of revenues, the total market for vaccines is considered small compared to pharmaceuticals. Moreover, the vaccine market in developing countries is characterized by unpredictability, slow adoption rates, and low prices.

In light of the costs, complexity, and uncertainty associated with vaccine development as well as the limitations of the markets, it is not surprising that vaccine research—particularly that aimed to benefit developing countries—is not supported at levels that optimize the probability of developing a successful vaccine rapidly. Because of the

importance of AIDS vaccines to global health, there is a clear need for strong public sector support for basic research and product development.

Basic research

More than a dozen countries already provide support for basic AIDS research (albeit at widely varying levels). Most notable among these are the U.S. National Institutes of Health (NIH) and the French Agence National de Recherche sur le SIDA (ANRS). Such support is critical for encouraging new medical breakthroughs and advances in both AIDS drug and vaccine development and must be continued and expanded.

Accelerated product development and clinical trial support

Public sector support for applied vaccine development and clinical trials is essential. Institutions that have most visibly provided support for product development and clinical testing of candidate AIDS vaccines are the NIH, the ANRS, the U.S. Walter Reed Army Institute for Research, and the U.K.'s Medical Research Council. Multilateral organizations that also support these efforts are the European Union and WHO/UNAIDS. In addition, international development agencies of the U.K., the Netherlands, Canada, Ireland, and the U.S., as well as the World Bank and UNAIDS have supported IAVI's research and development program.

Strengthening and accelerating vaccine product development efforts requires a range of activities to encourage additional private sector R&D activities

All of these efforts, while laudable, are not nearly enough. IAVI has determined that a meaningful global program to accelerate AIDS vaccine development will require at least US$ 1.1 billion *above* the current expenditures over the next seven years.[18]

This financing should support:

- *development of new AIDS vaccine concepts* applicable to non-industrialized countries; and
- *clinical trials* including head-to-head trials to prioritize choices of candidates for entry into efficacy trials and increased site capacity in developing countries (particularly for efficacy trials).

Although the public sector can address some of these needs by providing incentives to industry, others will require direct financial allocations from public budgets.

Accelerated product development Public agencies can make essential contributions to accelerating AIDS vaccine development. Yet most

[18] International AIDS Vaccine Initiative. *Scientific blueprint 2000: Accelerating global efforts in AIDS vaccine development.* (IAVI, 2000).

expertise in this area resides within the private sector. Therefore, strengthening and accelerating vaccine product development efforts, requires a range of activities to encourage additional private sector R&D activities, including direct financing through the creation of public-private partnerships.

Tax incentives are one mechanism sometimes used by the public sector to stimulate greater investment in R&D by private industry. The Research and Experimentation Tax Credit in the U.S., for example, provides private companies a 20 percent credit on research and development expenditures that exceed a base amount. In addition, human clinical trial costs linked to the development of "orphan drugs" benefit from a 50 percent tax credit in the U.S.

While studies have found these incentives to be effective in stimulating overall private sector research and research aimed at developing drugs for orphan diseases in industrialized countries, they have had only limited impact on research for AIDS vaccines and other diseases afflicting developing countries. The broad nature of the existing incentives do not redress the market incentives that cause firms to favor therapeutic products for industrialized countries over preventive products or those products that largely benefit developing countries.

Tax incentives for investment in AIDS vaccine development can complement other initiatives designed to promote the rapid development and availability of vaccines

The increasingly urgent need to strengthen and accelerate research on vaccines for major infectious killers in developing countries has prompted some industrialized countries to investigate creative use of R&D tax credits. Currently, the U.K. government is developing a proposal to use targeted tax credits to stimulate vaccine-related R&D. In the U.S., the Vaccines for the New Millennium Act has been reintroduced in the U.S. Congress and includes a provision for a tax credit on vaccine R&D. The Belgian government has also expressed interest in creating tax credits for investment in vaccine development.

Tax incentives for investment in AIDS vaccine development can complement other initiatives designed to promote the rapid availability of an effective vaccine. Any such efforts should ideally be harmonized across countries to avoid trade disputes and include the following elements:

- *Specific focus on high-priority diseases and preventive technologies* Because of the inherent differential in profit potential between diseases primarily affecting developing countries and those with major industrialized markets, tax credits should be designed specifically to reward companies that invest in research on diseases impacting poor countries. A similar argument justifies rewarding research on preventive technologies such as vaccines.
- *Flat credit* A flat tax credit reduces tax liability by a certain percentage on all qualifying research over a given period. By contrast, an incremental credit reduces tax liability only on increases in investment in research. Because R&D credits may be most useful as incentives to maintain and expand existing programs, a flat credit that

rewards sustained investment may be more appropriate than an incremental credit.

- *Research covered by credit* Incentives are needed to encourage vaccine research companies to move a broad range of AIDS vaccine candidates into human clinical trials. An R&D tax credit will be most effective if it provides incentives for both pre-clinical and clinical research. It may be appropriate to build in a certification process to ensure that tax credits on pre-clinical work are appropriately allocated.

In order to ensure that these incentives do not provide a competitive advantage to established firms, benefits must also be made available to biotechnology companies that are not currently profitable (and hence, have no tax liability). It is possible to design incentives so that companies with no current tax liability are allowed to carry forward credits for use in future (profitable) years or to "cash in" losses from R&D expenditures in the current year.

Clinical trial support Direct public sector support (financial and technical) for clinical trials capacity is also essential. Some new action in this regard is being started. For example, the European Commission is establishing a European Clinical Trials Platform that is intended to increase the number of, and coordination between, trials carried out in the public and private sectors and to do this in collaboration with developing countries. The NIH's HIV Vaccine Trial Network (HVTN) is also expanding its clinical trial capacity.

Direct public sector support—financial and technical—for clinical trials capacity is essential

Yet more is needed. In particular, the number of clinical trial sites in developing countries and the capacity of these, must be expanded to assure rapid testing of a vaccine that meets developing country needs. This requires investment today to assess the needs and concerns of the local community, build local human capacity, develop infrastructure, conduct baseline epidemiological studies, and address ethical issues.

Trials and their outcomes can also be improved through the expanded and earlier involvement of developing country scientists, researchers, and policy makers in trial designs. For example, protocols can be adjusted so that, beyond assessing efficacy, they also address specific health policy issues relevant to developing countries. This should constitute part of a more extended collaboration in research and access-related issues among developing countries and between developing and industrialized countries.

5 Speeding and improving regulatory processes

Every pharmaceutical or biological product that is tested in humans or enters wide use requires regulatory oversight to ensure quality, safety, and efficacy. Although this oversight is most evident when a product is approved for human use, it influences the product development process from its inception (affecting the design of pre-clinical and clinical trials) and continues to be important even after a product is widely available (post-licensing studies that track adverse events).

Such regulation is essential to protect public health and enable clinicians to make informed decisions. At present, however, regulatory systems are not appropriately geared to ensure the most rapid access possible (without compromising safety) to AIDS vaccines.

One worldwide standard for regulatory decisions is not advisable. Licensure of an AIDS vaccine in an industrialized country, for example, does not necessarily imply that such a vaccine is appropriate for all developing countries (such as a vaccine that is sub-type-specific). Conversely, the risk-benefit analysis for a new AIDS vaccine is different among different countries. A partially effective vaccine that has little appeal in a country with a low level of HIV prevalence might represent an important additional weapon in a country with high prevalence levels.

Swift uptake of a new vaccine in developing countries will require changes in regulatory systems

Notwithstanding the benefits of a decentralized approach to product regulation, differences in procedures and approaches can result in delays (companies phase their efforts to license products in different jurisdictions) and additional expenses (additional studies and dossier preparations).

Swift uptake of a new vaccine in developing countries will require changes in regulatory systems. To ensure an appropriate balance between the need to protect the public from unsafe products and the global imperative of widely deploying new AIDS vaccines soon after they become available, the global community must act quickly to implement the following regulatory reforms:

- *Focused dialogue on key questions* This should involve a broad group of regulators, including those from developing countries, and should aim at developing a consensus on key scientific questions (such as efficacy endpoints) related to approval of new AIDS vaccines. Already, the European Community has committed itself to support such a dialogue, but it must be joined in this effort by other national and international bodies. The World Health Organization should have the lead role in facilitating this process, but will require additional financial support to do so.

• *Streamlined submission processes* Progress has been made in standardizing the regulatory approaches in Europe, Japan, and the United States under the auspices of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals. However, more will need to be done and these efforts should include and be undertaken by all countries. It is desirable, particularly for life-saving products of global importance, that dossier requirements be as similar as is reasonable to permit simultaneous (and, if possible, electronic) submissions. In addition, the pooling of scientific and regulatory expertise among national regulatory authorities with similar epidemiological and population characteristics can be used to expedite common or parallel reviews among countries.

• *Fast track reviews* All national regulatory authorities should have an explicit expedited review process (no longer than 6 months) for drugs and vaccines for life-threatening conditions. Fast-track mechanisms, *de facto* or *de jure,* currently exist in the European Union and in the United States.

Another IAVI document, *Actions to avoid potential regulatory delays for vaccines against HIV/AIDS,*[19] can be referred to for more discussion on regulatory issues and recommendations for minimizing delays without compromising safety.

All national regulatory authorities should have an explicit expedited review process (no longer than 6 months) for drugs and vaccines for life-threatening conditions

6 Ensuring adequate manufacturing capacity

Building industrial capacity for biological production can be costly (more than US$ 100 million) and difficult because process scale-up is not straightforward. It requires time (four to five years) and regulatory supervision. The supply challenge is to create enough capacity for AIDS vaccines at the start so that global introduction need not be phased in over many years. Due to technical and economic factors, this is not clear-cut.

Experience with childhood vaccines has highlighted that economic factors contribute strongly to a delayed introduction in developing countries. Over time, production processes become more efficient, other suppliers may enter the market, and sales growth in industrialized markets may level, thereby driving producers to seek other markets and to reduce prices. Developing country interest increases as experience with a vaccine in other countries demonstrates

[19] Isbell, M.T. and Widdus, R. *Actions to avoid potential regulatory delays for vaccines against HIV/AIDS.* (IAVI, forthcoming).

its value and, in a manner that is generally linked to more favorable prices, new vaccines are gradually adopted over a period of many years. A vaccine against hepatitis B has been available since 1981. While the price has dropped dramatically (more than 100-fold), today, approximately 60 percent of the world's children still do not receive this potentially life-saving vaccine.

Rapid, equitable access to AIDS vaccines clearly cannot be achieved in this way. While the previous sections have focused on speeding product availability and ensuring adequate economic demand, it is vital to recognize that these actions will fail to achieve access if supply is inadequate.

The most effective actions to stimulate adequate supply—the commitment of substantial, credible financing for vaccine purchase and the development of reliable demand estimates[20]—*must* be taken well in advance of product availability. While these actions might be sufficient for many other products, more will be needed to stimulate adequate supply of AIDS vaccines.

The challenge is to create enough manufacturing capacity for AIDS vaccines so that global introduction need not be phased in over many years

If the actions outlined in this paper are adopted by the public sector, then AIDS vaccine producers will be confronted with a demand curve that differs dramatically from the norm. In contrast to most childhood vaccines, where overall demand has grown gradually, global demand for AIDS vaccines is likely to experience very high growth at the start, followed by a decline and stabilization at lower maintenance levels. This demand will be based primarily on the need to deliver vaccines to adolescents and high-risk adults. Reliable demand estimates will clearly be needed. Additionally, for vaccines of modest efficacy, there is the risk that the entry of a competing product with improved efficacy will swiftly diminish the first product's market share.

Decisions by producers, and their lenders, regarding production capacity are not made in a vacuum. Investment alternatives are compared to each other in terms of cost and likely returns. Even with favorable financing, markets for AIDS vaccines may not yield sufficiently high returns relative to other investments. Moreover, with a compressed research and development timeline, manufacturing decisions may need to be taken even earlier than usual to ensure timely product availability. This increases the financial risk that a firm is exposed to. Some assistance in overcoming these financial challenges is likely to be required.

While it is difficult to devise exact solutions to a problem that requires further specification, the public sector should demonstrate a

[20] As previously mentioned, demand estimates are being made through a joint IAVI-WHO-UNAIDS project and a complementary World Bank project funded by the EC.

willingness to work with the private sector to ensure that sufficient capacity is put in place early enough to meet global demand for AIDS vaccines.

Some options for consideration that involve public sector action include:

- Expanded use of existing loans and loan guarantees such as those provided by the European Investment Bank, the Overseas Private Investment Bank (U.S.), KfW (Germany), the Japan Bank for International Cooperation (Japan), and the International Finance Corporation (World Bank).
- Creation of new mechanisms to provide public sector financing or subsidies for manufacturing facilities designed to produce AIDS vaccines for developing countries. These could include accelerated depreciation for manufacturing facilities, or issuance of revenue bonds for construction.
- Additional public sector payments on initial orders to enable companies to rapidly retire debt on construction of manufacturing facilities.
- Creation of novel loan guarantees extended to firms that agree, for example, to produce a specific number of doses and over a specified time period.
- Facilitation of licensing and technology transfer agreements that respect patent rights but would permit other producers (public or private) to provide additional capacity under specified conditions.
- Construction of a public facility that could be contracted to a producer for a limited period of time to cover demand that significantly exceeds global maintenance levels.

The public sector should demonstrate a willingness to work with the private sector to ensure that sufficient capacity is put in place early enough to meet global demand for AIDS vaccines

7 Conclusion

The new paradigm for access proposed in this paper differs from the existing one in three key ways:

1 Access is not viewed as "tomorrow's problem." Plans and actions leading to rapid introduction of essential health products must be made well in advance of product availability. This requires a shift from the current paradigm that effectively treats access as a problem to be "fixed" long after the trouble has become apparent, rather than as an objective to be achieved from the start.

2 An integrated approach covering a range of areas and including new interventions is undertaken. Current access activities and mechanisms do not suffice. For example, an AIDS Vaccination Fund can provide what existing *ad hoc* financing mechanisms cannot—a credible

assurance of adequate financing that not only will serve countries when a vaccine becomes available, but also offers incentives to countries (to plan) and industry (to invest). Access is a multi-faceted issue. Therefore, a focus only on one aspect will not achieve the desired results. Coordinated action on a "package" of interventions impacting research and development, regulatory processes, manufacturing, financing, pricing, and delivery systems is essential.

3 New forms of participation and cooperation are created. This involves far more than extended involvement by industrialized countries in matters of global health.

More involvement by developing countries in the processes and mechanisms that lead to access is required. For example, such countries must be key partners in any effort to devise global financing structures and be represented in the bodies that govern these. They should also begin working on policies for vaccine use that will lead to better estimates of demand and earlier, more effective product introductions. Developing countries *must also work with each other,* not just with industrialized nations, on the full range of issues that determine access. It has been suggested in this paper, that consideration be given to the establishment of regional regulatory networks by which countries can share expertise and harmonize processes to expedite product reviews.

The active involvement of the private sector, affected communities, individuals with HIV/AIDS, and the larger civil society is crucial, and the public sector should act to catalyze and coordinate, as well as to contribute to, this expanded collaboration

While this paper has focused on public sector actions, it is clear that the public sector alone cannot assure access to AIDS vaccines. The active involvement of the private sector, affected communities, individuals with HIV/AIDS, and the larger civil society is also crucial. The public sector should act to catalyze and coordinate, as well as to contribute to, this expanded collaboration.

A preventive AIDS vaccine represents the world's best hope for halting the pandemic. It also represents a chance for the world to change its approach to access. With millions of lives hanging in the balance, this is an opportunity that the global public sector cannot afford to miss.

A1 Recommended actions for industrialized countries, developing countries, and multilateral institutions

Industrialized countries should:

- Give the AIDS pandemic the priority it deserves both within their own countries as well as globally. This means allocating new and significant resources (financial, technical, and human) to global efforts to combat AIDS.
- Create now, together with other parties, a global health or AIDS fund that includes a separate account for AIDS vaccines. Billions of dollars will be required annually if a fund is to adequately address global health emergencies. Make firm, and substantial commitments to necessary financing—in the billions of dollars—for the AIDS vaccine account when these products become available.
- Through the global fund and other mechanisms, begin now to address infrastructure and delivery issues relevant to AIDS therapeutics and vaccine delivery.
- Explicitly support tiered pricing, and enact adequate and enforced controls against import of health products purchased under such a scheme by lower price markets.
- Work together to create tax relief for firms providing appropriate vaccine donations, harmonized among relevant countries. Such donations, however, should not be seen as substitutes for adequate financing and developing tiered pricing. In addition, donations should meet internationally agreed safety and quality standards.
- Substantially increase direct support for research and development of AIDS vaccines. Ensure that this is done, wherever possible, in partnership with affected developing countries.
- Create incentives for private industry to invest in AIDS vaccine research, development, and production capacity to address global needs.
- Harmonize and speed regulatory processes.

Developing countries should:

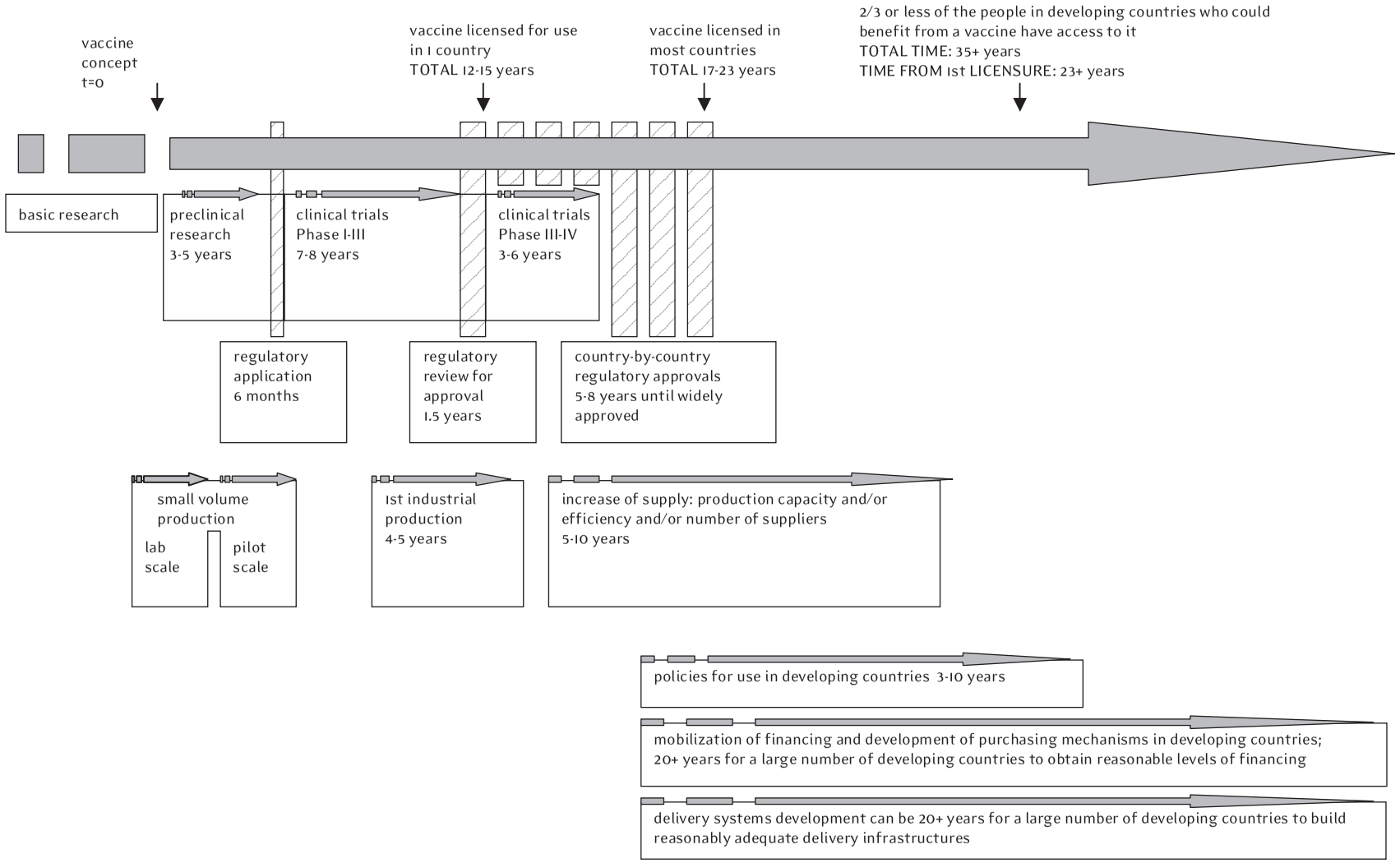
- Continue, expand, and intensify all efforts to improve health systems, including the delivery of essential health products.
- Give the AIDS pandemic the high priority it requires and assign national resources in proportion to this.

- Engage in the creation and governance of any global health/AIDS fund and promote the allocation of a separate account for AIDS vaccines within this.
- Support tiered pricing through adequate and enforced controls against export of health products purchased under such a scheme to higher price markets (and away from the intended beneficiaries).
- Enhance South-South and North-South collaboration in research and development; this includes becoming active partners in efforts to expand clinical trial capacity and ensuring that all trials adhere to agreed ethical standards.
- Work together to ensure that all countries have access to joint purchase or price negotiation mechanisms (grouping countries of similar need and economic situation).
- Harmonize and speed regulatory processes.

Multilateral institutions should:

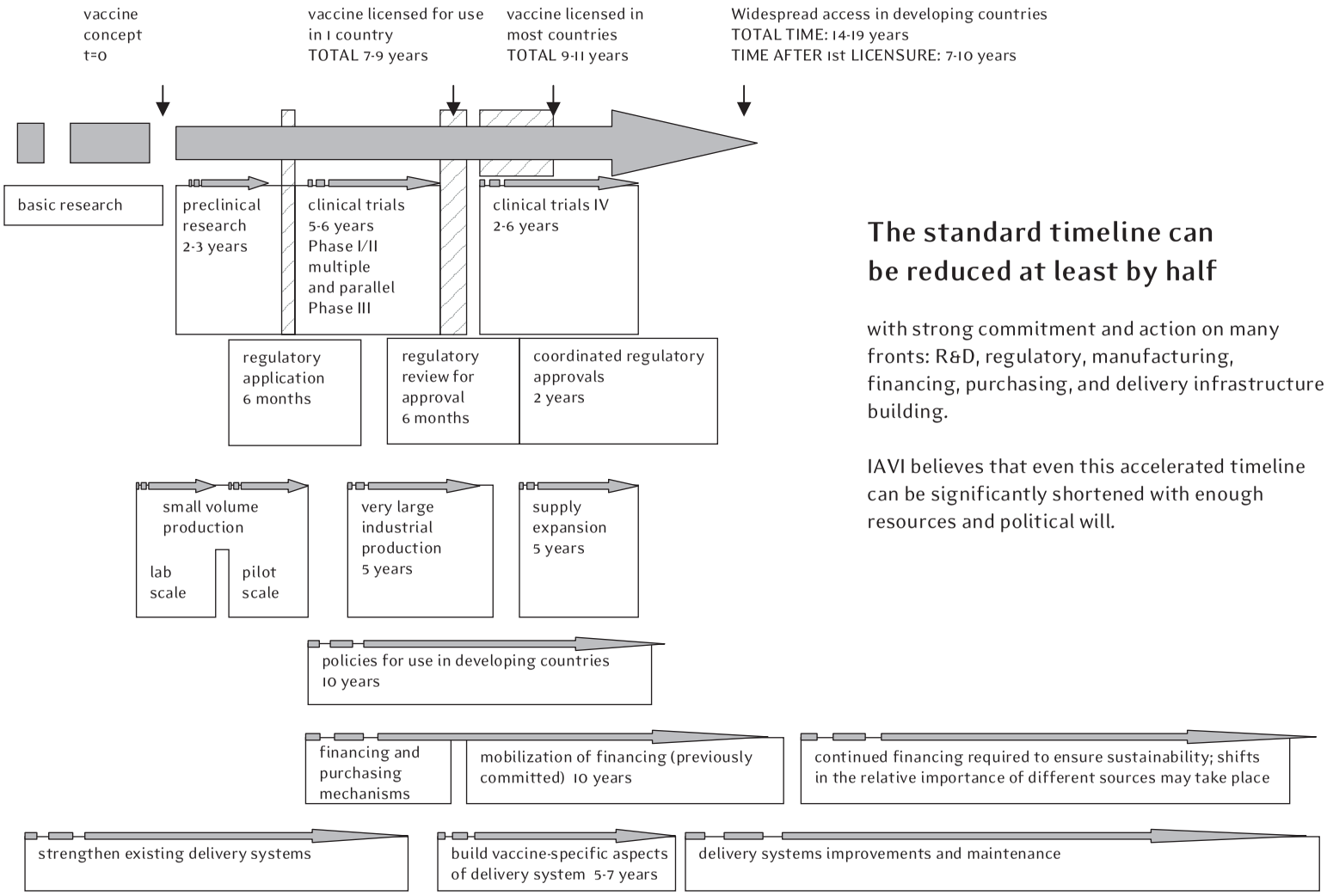
- Expand financial and technical support to countries to strengthen health sectors and AIDS programs.
- Coordinate roles and work together and with other parties to ensure that any global financing architecture for AIDS and for AIDS vaccines is coherent, efficient, and well-managed.
- Begin now to address infrastructure and delivery issues relevant to AIDS vaccine delivery.
- Provide clear support for tiered pricing and technical support, should it be required, for implementing it.
- Support developing countries, should this be requested, in creating appropriate joint procurement and/or price negotiating systems.
- Allocate financial support to AIDS vaccine research and development in a manner that properly reflects the priority of this issue.
- Work closely with countries to help coordinate collaboration in research and development, regulatory matters, and access issues.

A2 Typical timeline for vaccine development and access[21]



[21] Adapted from information in *AIDS vaccines for the world: Preparing now to assure access* (International AIDS Vaccine Initiative, 2000); and *Scientific Blueprint 2000: Accelerating global efforts in AIDS vaccine development* (International AIDS Vaccine Initiative, 2000).

A3 Proposed timeline for AIDS vaccine development and access[22]



The standard timeline can be reduced at least by half

with strong commitment and action on many fronts: R&D, regulatory, manufacturing, financing, purchasing, and delivery infrastructure building.

IAVI believes that even this accelerated timeline can be significantly shortened with enough resources and political will.

[22] Adapted from information in *AIDS vaccines for the world: Preparing now to assure access* (International AIDS Vaccine Initiative, 2000); and *Scientific Blueprint 2000: Accelerating global efforts in AIDS vaccine development* (International AIDS Vaccine Initiative, 2000).

A4 Existing situation and mechanisms supporting access to AIDS vaccines

To assure access for	Finance for product purchase and delivery infrastructure	Price/Procurement	Regulatory: enhancing capacity and improving efficiency	Research and product development	Manufacturing capacity
Advanced economies	Provided by a mix of public and private financing and delivery systems.	Mix of public and private purchase mechanisms.	Fast-track approval mechanism in the U.S. and Europe.	Several countries providing public sector research support. The largest of these is the NIH (U.S.). Nonetheless, the resources are inadequate, particularly regarding product development and expensive efficacy trials. Number and capacity of efficacy trial sites in developing countries is very limited. R&D tax credits offered by the U.S.	Market incentives likely to produce enough capacity for these markets.
Mid-income developing countries	Some (but not sufficient) financing from national resources should be possible with political will. Possible to obtain loan financing; likely that some bilateral assistance mechanisms will be extended. These are inadequate without coordination and substantial expansion.	PAHO procurement mechanism exists for Latin American countries.			Market incentives will not produce enough capacity for these markets. Some public sector mechanisms (IFC, EIB, etc.) offer attractive loans for building additional capacity.
Low-income developing countries	Very inadequate financing available from national sources. Possible to obtain loan financing; likely that some bilateral assistance mechanisms will be extended, but these are inadequate without coordination and substantial expansion. GAVI (GFCV) financing may be possible, but not currently adapted for this.	UNICEF procurement mechanism exists for the purchase of "underutilized" vaccines for the poorest countries.			

What (in addition) is needed to assure access to AIDS vaccines

To assure access for	Finance for product purchase and delivery infrastructure	Price/Procurement	Regulatory: enhancing capacity and improving efficiency	Research and product development	Manufacturing capacity
Advanced economies	Sufficient additional financing to meet population needs.[23] Strengthening of delivery systems.	Price (and financing to pay for it) high enough to provide an adequate return on private sector investment.[24] Mechanisms to avoid re-importation.	Agreement by regulatory agencies on the scientific issues relevant to approval processes. Agreement on means to better coordinate submissions and approvals. Widespread fast-track capacity.	US$ 1.1 billion more in spending over the next 7 years, focusing on applied product development, particularly on products for developing countries. Financial and technical support for clinical trials (particularly efficacy trials in developing countries). Harmonized (across countries with private sector R&D capacity) tax incentives for R&D.	
Mid-income developing countries	Substantial, credible financing[25] from the international community provided through a streamlined mechanism to speed introduction and cover catch-up costs. Substantial additional domestic financing dedicated to HIV/AIDS prevention including vaccines.	Price must be tiered to be lower than that in industrialized countries. Mechanisms to avoid export to higher-priced markets. Expand/create regional procurement mechanisms so that every country has this option open to it.	Agreement by regulatory agencies on the scientific issues relevant to approval processes. Widespread fast-track capacity linked to regional[26] coordination that allows for a common or parallel submission and approval process.		Explore options: Expand existing public loan mechanisms. Provide limited public sector loan guarantees for commercial loans. Create government owned-contractor operated facilities that can help meet fluctuations in demand.

[23] Required to ensure access to individuals in these countries, but also to support social acceptance of tiered pricing.

[24] Adequate revenue from industrialized country markets is a prerequisite for the ability of commercial manufacturers to tier product prices.

[25] "Substantial financing" implies an ability to extend grants of a *minimum* US$ 1 billion per year.

[26] Grouping of countries with similar epidemiological and population characteristics.

To assure access for	Finance for product purchase and delivery infrastructure	Price/Procurement	Regulatory: enhancing capacity and improving efficiency	Research and product development	Manufacturing capacity
Low-income developing countries	Very substantial, credible financing from the international community for at least 2 decades to cover vaccine and delivery costs. Additional domestic financing dedicated to HIV/AIDS prevention including vaccines.	Price must be tiered to be substantially lower than that in industrialized countries. Mechanisms to avoid export to higher-priced markets. Harmonized tax incentives for donations. Ensure sufficient capacity through UNICEF mechanisms or other procurement mechanisms.	See above	See above	See above

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