

UNAIDS Questions & Answers provide information on UNAIDS, its work and issues related to the AIDS epidemic.

Q&A II: Selected issues: prevention, care and funding

Section I: Prevention

Section II: Injecting drug use

Section III: HIV vaccines

Section IV: Microbicides

Section V: Condoms and safer sex

Section VI: Religious organizations and the response to HIV/AIDS

Section VII: Mother-to-Child Transmission

Section VIII: HIV Testing

Section IX: Care, treatment and support

Section X: Resources

PEPFAR

- The Global Fund to Fight AIDS, Tuberculosis and Malaria
- The Heavily Indebted Poor Country Initiative (HIPC)
- The Multi-Country HIV/AIDS Program for Africa (MAP)

Section I: Prevention

I/1 What have been the elements of successful prevention campaigns and what are some examples where these have occurred?

Much has been learned in the how best to control the spread of HIV since the start of the epidemic. HIV prevention has led to decreases in the incidence of HIV infection in numerous populations such as among men who have sex with men in many Western countries, among young women in Uganda, among young men in Thailand and among injecting drug users in Spain and Brazil. More and more countries have made headway against their epidemics through prevention efforts, including Cambodia, Kenya and Zimbabwe, where surveillance has documented notable declines in the prevalence of HIV.

The UNAIDS *Intensifying HIV prevention* policy position paper, endorsed by the UNAIDS Programme Coordinating Board in June 2005 has identified 12 essential policy actions for HIV Prevention which follows:

1. Ensure that human rights are promoted, protected and respected and that measures are taken to eliminate discrimination and combat stigma.
2. Build and maintain leadership from all sections of society, including governments, affected communities, non-governmental organizations, faith-based organizations, the education sector, media, the private sector and trade unions.
3. Involve people living with HIV in the design, implementation and evaluation of prevention strategies, addressing their distinct prevention needs.
4. Address cultural norms and beliefs, recognizing both the key role they may play in supporting prevention efforts and the potential they have to fuel HIV transmission.
5. Promote gender equality and address gender norms and relations to reduce the vulnerability of women and girls, involving men and boys in this effort.
6. Promote widespread knowledge and awareness of how HIV is transmitted and how infection can be averted.
7. Promote the links between HIV prevention and sexual and reproductive health.
8. Support the mobilization of community-based responses throughout the continuum of prevention, care and treatment.
9. Promote programmes targeted at HIV prevention needs of key affected groups and populations.
10. Mobilizing and strengthening financial and human and institutional capacity across all sectors, particularly in health and education.
11. Review and reform legal frameworks to remove barriers to effective, evidence based HIV prevention, combat stigma and discrimination and protect the rights of people living with HIV or vulnerable or at risk to HIV.
12. Ensure that sufficient investments are made in the research and development of, and advocacy for, new prevention technologies.

There are also 11 essential programmatic actions in the policy position paper and these are the following:

- Prevent the sexual transmission of HIV,

- Prevent mother-to-child transmission of HIV,
- Prevent the transmission of HIV through injecting drug use, including harm reduction measures,
- Ensure the safety of the blood supply,
- Prevent HIV transmission in healthcare settings,
- Promote greater access to voluntary HIV counseling and testing while promoting principles of confidentiality and consent,
- Integrate HIV prevention into AIDS treatment services,
- Focus on HIV prevention among young people,
- Provide HIV-related information and education to enable individuals to protect themselves from infection,
- Confront and mitigate HIV-related stigma and discrimination, and
- Prepare for access and use of vaccines and microbicides.

I/2 How are prevention achievements measured?

Success is measured using the targets for HIV prevention established by governments in the 2001 United Nations General Assembly Special Session *Declaration of Commitment on HIV/AIDS* which are as follows.

- *Para 47. By 2003, establish time-bound national targets to achieve the internationally agreed global prevention goal to reduce by 2005 HIV prevalence among young men and women aged 15 to 24 in the most affected countries by 25% and by 25% globally by 2010, and to intensify efforts to achieve these targets as well as to challenge gender stereotypes and attitudes, and gender inequalities in relation to HIV/AIDS, encouraging the active involvement of men and boys;*
- *Para 52. By 2005, ensure: that a wide-range of prevention programmes that take account of local circumstances, ethics and cultural values, is available in all countries, particularly the most affected countries, including information, education and communication, in languages most understood by communities and respectful of cultures, aimed at reducing risk-taking behaviour and encouraging responsible sexual behaviour, including abstinence and fidelity; expanded access to essential commodities, including male & female condoms and sterile injecting equipment; harm-reduction efforts related to drug use; expanded access to voluntary and confidential counseling and testing; safe blood supplies; and early and effective treatment of sexually transmissible infections;*
- *Para 54. By 2005, reduce the proportion of infants infected by HIV by 20% and by 50% by 2010, by ensuring that 80% of pregnant women accessing antenatal care have information, counseling and other HIV prevention services available to them, increasing the availability of and providing access for HIV-infected women and babies to effective treatment to reduce mother-to-child transmission of HIV, as well as through effective interventions for HIV-infected women, including voluntary counseling and testing, access to treatment, especially antiretroviral therapy, and, where appropriate, breast-milk substitutes and the provision of a continuum of care;*

- *Para 58. By 2003, enact, strengthen or enforce, as appropriate, legislation, regulations and other measures to eliminate all forms of discrimination against and to ensure the full enjoyment of all human rights and fundamental freedoms by people living with HIV/AIDS and members of vulnerable groups, in particular to ensure their access to, inter alia, education, inheritance, employment, health care, social and health services, prevention, support and treatment, information and legal protection, while respecting their privacy and confidentiality; and develop strategies to combat stigma and social exclusion connected with the epidemic;*
- *Para 65. By 2003, develop and by 2005 implement national policies and strategies to build and strengthen governmental, family and community capacities to provide a supportive environment for orphans and girls and boys infected and affected by HIV/AIDS, including by providing appropriate counseling and psychological support, ensuring their enrolment in school and access to shelter, good nutrition and health and social services on an equal basis with other children; and protect orphans and vulnerable children from all forms of abuse, violence, exploitation, discrimination, trafficking and loss of inheritance.*

I/3 What is comprehensive programming for HIV prevention?

To be successful, HIV prevention must utilize all approaches known to be effective, not implementing exclusively one or a few select actions in isolation. Comprehensive HIV prevention programmes benefit from the full range of up-to-date scientific information concerning transmission and the measures that can be adopted to protect against infection. These should be offered to individuals and communities in a frank, non-discriminatory and open manner. Comprehensive programming should also be multisectoral in approach, recognizing the importance and value added of effectively engaging all relevant sectors. This programming should link with poverty reduction strategies. It also includes a broader focus on sexual and reproductive health, comprehensive and appropriate sexual education, life skills, drug-related education, work-place education, school-based education, and linkages with existing programmes in all sectors.

Most importantly, a comprehensive approach to HIV prevention must address not only risk but also deep-seated causes of vulnerability which reduce the ability of individuals and communities to protect themselves and others against infection. This necessitates providing for instance, more opportunities and greater equity in education and employment for women, young people and marginalized populations, who are particularly vulnerable to HIV; enabling families to maintain their homes and property when disability or death occurs; food security programmes especially for vulnerable young people and women; and specific protection measures for refugees and people in conflict and displaced populations.

I/4 Why is it essential to integrate HIV prevention programming and care, treatment and support?

The majority of people living with HIV in low- and middle-income countries are not aware of their HIV infection. Increased provision of treatment and care services will help motivate people to be tested. This, in turn, requires increased availability of voluntary counseling and testing services (VCT). VCT stands at the heart of prevention and treatment. Behavioural counseling and provision of condoms, clean needles and syringes must be made available to people, irrespective of their HIV status. After testing positive, people living with HIV can be

offered care, treatment and support services, including ARV if necessary. Counseling and other services aimed at prevention of secondary transmission, as well as the provision of ARV to prevent mother-to-child transmission, are an essential component of follow-up services for individuals who test positive. Effective prevention programming and treatment, care and support services therefore go hand-in-hand.

Mathematical modeling by Salomon, et al. (2005) comparing a range of scenarios show that in the scenario in which effective HIV prevention and treatment are scaled up jointly, the benefits, both in terms of new HIV infections and deaths averted are greatest. The conclusions of this study are clear:

- Successful HIV treatment can enable more effective HIV prevention;
- Intensified HIV prevention is needed to make HIV treatment affordable and sustainable; and
- Sustained progress in the response against AIDS will only be attained by intensifying HIV prevention and treatment simultaneously.

Section II: Injecting drug use

The sharing of non-sterile injecting drug equipment remains one of the critical activities fuelling the epidemic among drug users and beyond them in many parts of the world. To stop this form of transmission, a comprehensive package of interventions must be mounted to reach out to injecting drug users and their partners. Such a package should include "harm reduction" activities, such as information and education, needle-syringe exchange, condoms, substitution treatment and treatment of sexually transmitted infections (STIs), as well as "demand reduction" activities. Programmes must be supported by clear authorization and sufficient funding to enable them to go to scale.

II/1 What is the best way to prevent HIV transmission through injecting drug use?

HIV transmission through injecting drug use is best prevented by providing a comprehensive package of interventions and services in outreach to injecting drug users (IDUs) and their injecting or sex partners. Any single activity on its own will not work. Critical HIV prevention measures among drug users include:

- Provision of HIV information and education to drug users and their sex partners about HIV risks and about safer injecting and safer sexual practices;
- Making condoms available to drug users;
- Needle-syringe exchange programmes;
- Integration of HIV prevention and care into drug (addiction) treatment programmes;
- Provision of counselling, care and support for drug users living with HIV infection or AIDS;
- Access to treatment for sexually transmitted infections and other health care services for drug users and their partners;
- Substitution treatment.

II/2 What are "harm reduction" and "demand reduction"?

The measures described above have at times been called 'harm reduction' in that they are aimed at reducing at least one harm associated with injecting drug use, that of HIV transmission among drug users and beyond. 'Demand reduction' programmes aim to dissuade people from using drugs in the first place, i.e. to reduce the number of IDUs within the population.

Harm reduction and demand reduction programmes should be conducted together, but in ways that allow each approach to be effective. There needs to be clear government policy and legislation that authorizes each type of programme and related activities, as well as sufficient funding so that they can be carried out on a sufficiently large scale. An example of a developing country that has set up appropriate policies and laws in this field is Brazil, where they have helped achieve substantially lower HIV prevalence rates among IDUs in several cities.

II/3 Is there a risk that needle/syringe exchange programmes might "send the wrong message" and result in more injecting drug use?

The evidence does not support this view. Studies conducted in Australia, Canada, Sweden, the UK and the USA have all shown that needle/syringe exchange programmes—particularly when carried out in concert with other interventions—help reduce the sharing of injecting equipment and the transmission of HIV. There was no evidence that needle exchange programmes increased either the number of people using drugs or the frequency of injecting drug use.

The effectiveness of harm reduction programmes in reducing HIV infections among people who inject drugs is evident in several countries. In Portugal, for example, HIV diagnoses among injecting drug users were almost one third (31%) lower in 2005, compared with 2001 (857 versus 1247) (EuroHIV, 2006a). Harm reduction programmes have been associated with a decrease in injecting drug use, use of contaminated needles and syringes and HIV infections among injecting drug users in Spain. HIV prevalence among injecting drug users declined by half in Barcelona (44% to 21% between 1995 and 2001–2003) and Sevilla (44% to 22%), both cities with long-standing harm reduction programmes.

However, research in Canada has highlighted the limitations of some needle/syringe-exchange programmes. For example, studies in Vancouver and Montreal, where cocaine injection is prevalent, have shown the importance of tailoring programmes to meet local conditions. Cocaine injectors tend to inject much more frequently than heroin injectors, and therefore require much greater quantities of sterile needles and syringes than usually provided by most needle-exchange programmes.

Another current limitation of needle-exchange and other interventions targeting drug users is that they often miss occasional or recreational drug users. This is an increasingly important issue, especially among young people, as this population is missed by many programmes targeting self-identified injecting drug users.

Section III: HIV vaccines

A future HIV vaccine will not be a "magic bullet". But future vaccination against HIV, applied alongside prevention measures focused on safer behaviour, male and female condoms, a potential microbicide, STI control, and possibly male circumcision, holds out realistic hope

for ending the HIV epidemic. HIV vaccine development is unusually challenging for reasons that relate to the virus itself, ethical considerations in the conduct of vaccine trials, and the multiple social, financial and logistical aspects of developing the necessary capacities, human resources and infrastructures required for preparation and implementation of multiple clinical trials, in particular in low- and middle-income countries.

III/1 Will it be possible to develop a vaccine for HIV?

We remain optimistic with regard to this question. In a small number of experiments, protection of animals against AIDS-like disease with a vaccine has been reported, but it remains uncertain as to whether that success can be extrapolated to humans. The search for an HIV vaccine therefore has to include laboratory and animal experiments, as well as human clinical trials which are costly and time-consuming.

III/2 Why is it taking so long to develop an HIV vaccine?

The peculiarities of the human immunodeficiency virus make the development of an HIV vaccine a difficult and expensive process. For most infectious diseases, a successful vaccine stimulates an effective immune response in order to protect the body and help it recover from disease. But HIV immobilizes the body's immune responses and leaves them incapable of controlling infection or preventing disease. Furthermore, traditional vaccine strategies exploit the use of an entire micro-organism (virus or bacterium) that has been killed or rendered harmless, such is the case with smallpox, polio, measles and other vaccines. In the case of HIV, however, this approach is not considered safe, and experimental HIV vaccines are based on parts of the virus to make absolutely sure that vaccination does not result in HIV infection. This makes the development of a vaccine even more challenging. In addition, HIV is very variable (as is the virus responsible for flu), and it is not known whether a vaccine protecting against one subtype of HIV would also protect against the other subtypes.

III/3 Will it be necessary to develop a vaccine for each genetic subtype of HIV?

First of all, it should be noted, that the genetic classification of HIV-1 into various subtypes and various recombinant forms does not necessarily predict the biological and immunological properties of the virus. Therefore, it remains uncertain what would be the most sensible strategy to use in attempting to match vaccine candidates to the types of the virus circulating in populations where an effective vaccine will eventually be used. However, it would clearly be desirable to have an HIV vaccine that would be effective against all subtypes of HIV. That, coupled with the fact that the subtypes in developing countries differ from those prevalent in the industrialized world, makes it essential that experimental vaccines be developed simultaneously in high-income and low-income countries, and in different regions of the world. The practical approach adopted by the majority of HIV vaccine experts exploits the development of candidate vaccines based on globally prevalent HIV strains, such as subtypes C, A and B. Those candidate vaccines are then evaluated in specially designed efficacy trials in order to measure the efficacy of the vaccine in protecting individuals against different subtypes. The WHO-UNAIDS Virus Network serves as an important source of epidemiologically relevant HIV strains and related vaccine reagents for

the development of various candidate HIV vaccines, suitable for testing and eventual use on a global basis, especially in developing countries.

Information on prevalent sub-types can influence the development and testing of specific vaccine products. For example, in Thailand when molecular epidemiologists reported that the dominant subtype B had been replaced with another—subtype E—in a population of injecting drug users among whom the trial was to be conducted, the vaccine makers modified the vaccine to include two different vaccine components so as to target both subtypes.

III/4 What is the difference between Phase I, II and III trials?

Phase I trials involve 20-40 low risk volunteers. They are intended to confirm the vaccine's safety and determine whether it triggers HIV-specific immune responses. Phase II tests can involve up to hundreds of volunteers and are intended to further check vaccine safety and assess the potency of the immune responses and to determine the optimal vaccine dose, route of administration and vaccination schedule. Phase III trials are large-scale field trials involving thousands of volunteers who are randomized to receive the vaccine candidate or an inert placebo. The aim is to determine efficacy of the candidate vaccine, i.e. gauge whether the candidate vaccine can indeed protect people against HIV infection or, if they become infected despite having received the vaccine, whether the candidate vaccine protects against disease progression and the onset of AIDS. Moving vaccines through the three phases can take up to five years or more.

III/5 Have HIV vaccines already been tested in humans?

Yes, around 30 different HIV candidate vaccines have been tested since 1987 in over 80 phase I/II clinical trials, involving more than 10 000 human volunteers free from HIV infection. Most of these trials have been conducted in the US and Europe, but some have been held in developing countries (Botswana, Brazil, China, Cuba, Haiti, India, Kenya, Peru, South Africa, Thailand, Trinidad and Tobago, and Uganda). The aim of Phase I/II trials is to assess candidate vaccines with regard to their safety and their immunogenicity (that is, the vaccine's ability to induce an immune response against HIV).

To date only two large-scale Phase III efficacy trials have been completed: one in the US, involving 5,000 men who have sex with men (MSM), and one in Thailand among 2,500 injecting drug users (IDUs) This vaccine candidate was produced by VaxGen, a US-based biotechnology company. The vaccine strategy pursued by this company was based on the use of gp120 (an external protein of HIV called a glycoprotein) which plays a major role in the attachment of the virus on to the surface of the target human cells and thus the use of this protein as part of the vaccine was expected to induce the production of antibodies capable of neutralizing the virus. VaxGen has developed two types of gp120 candidate vaccine. Both of them are bivalent (they contain HIV glycoproteins from two different HIV strains). The one tested in the USA is based on two different strains of HIV subtype B, the sub-type that is prevalent in the Americas, Western Europe, Australia, and New Zealand. The other vaccine candidate was modified to include rgp120 derived from subtypes B and E, both of which are prevalent among injecting drug users in Bangkok, among whom the vaccine efficacy was tested.

Results from the Phase III clinical trial in Thailand, released in November 2003, revealed that the vaccine candidate did not show efficacy for either the primary or secondary endpoints. The primary endpoint for the trial was the prevention of infection by HIV, the virus that causes AIDS. The secondary endpoint was slowing of disease progression among those who received the vaccine but later became infected with HIV. Likewise, the results of the subtype B trial in the US did not demonstrate any significant level of efficacy.

On the other hand, these trials should be viewed as an important step forward since for the first time they have produced definitive answers to a number of key scientific and logistic challenges that are required to move forward the whole field of HIV vaccine development.

A third large-scale community-based phase III trial, using a prime-boost regime (priming with a Canary pox-HIV vector followed by gp 120/Vaxgen boost), started in 2003 and is under way in Thailand with 16 000 participants. Results are expected to be available by 2007-08. These trials will produce valuable information, regardless of the success or failure of the vaccine candidate itself. That information will enable us to move ahead in the search for an effective vaccine. Several other candidate HIV vaccines are under development and may possibly enter phase III efficacy trials in between 2008 and 2010. These are based essentially on attenuated or non-replicative viral vectors (poxviruses, adenoviruses, among others) and are meant to protect against disease more than against infection.

III/6 What type of trials are needed to see if a vaccine actually works?

Large-scale Phase III trials are the only trials that can provide definitive information on the efficacy of protection. These are field trials conducted in populations with a relatively high incidence of naturally-occurring HIV infection (usually more than 1% per year). Half the volunteers receive the candidate vaccine and half receive a control injection. All receive HIV prevention counselling. To avoid biases in the interpretation of the results, neither the volunteers nor the investigators know who is receiving which. This is known as a double-blind controlled trial. The population, usually several thousand volunteers (depending on HIV incidence), is tracked for 2-4 years to see if fewer of the vaccinated volunteers become infected with HIV than the control volunteers.

III/7 If you need to have a certain rate of HIV infection to assess the efficacy of the vaccine, would you encourage people to be exposed to the virus?

Of course, not. That would be unethical. It is an absolute requirement that populations enrolled in HIV vaccine efficacy trials should be counselled on how to avoid exposure to HIV and provided with the means to prevent HIV acquisition relevant to their likely exposure route, such as male and female condoms, sterile injecting equipment, etc. They are told that nobody knows if the vaccine will work, and that they should continue to practice or should adopt low-risk practices. Nevertheless, we know that 'behavioural' prevention programmes are not 100% effective and that some residual risk of HIV acquisition will remain. That residual level of HIV infection is what allows vaccine efficacy to be gauged.

III/8 What are some of the other vaccine initiatives that are underway?

At present, a whole new generation of candidate HIV vaccines are under development, in particular those based on globally prevalent HIV strains, which may be more appropriate for use in developing countries. These candidate vaccines are developed under frameworks of

different national agencies in private and public sectors, including among others the US National Institutes of Health (NIH), European research institutions, the International AIDS Vaccine Initiative (IAVI) and the European and Developing Country Clinical Trials Partnership (EDCTP), as well as an increasing number of national HIV vaccine programmes and research institutions in developing countries. WHO, UNAIDS and the African AIDS Vaccine Programme (AAVP) are committed to supporting developing countries in building capacity to conduct clinical trials of the highest scientific and ethical standards. The Global HIV Vaccine Enterprise endorsed by the G-8 countries (see question 12 below) is also providing a new and vital boost to help forge the strategic planning and global investment of resources by governments and industry that is commensurate with the intensive effort required to develop a globally accessible and affordable HIV vaccine.

III/9 What is being done to ensure that trials are conducted with the appropriate scientific and ethical standards?

In 2000, UNAIDS issued a Guidance Document on 'Ethical considerations in HIV preventive vaccine research', which was developed through an intensive process of international consultation. The WHO-UNAIDS HIV Vaccine Initiative facilitates the provision of technical support provision in this area and conducts training workshops to strengthen the capacity of developing countries, particularly in Africa through the African AIDS Vaccine Programme (AAVP), to conduct ethical reviewing.

III/10 Would a successful vaccine mean we can abandon other prevention programmes?

No. A vaccine will not be a panacea, nor can it be an alternative to existing methods for preventing HIV spread through sex, blood or drug use. Because an eventual vaccine is unlikely to be 100% effective, it will join other prevention methods as an additional method within comprehensive HIV prevention programming, but not one that should replace other more effective means of reducing HIV infection, such as abstinence, sex between people who are both HIV negative, and the use of male and female condoms. In fact, once a vaccine is developed, awareness-raising and prevention efforts will need to be redoubled in order to counter the risk of complacency.

III/11 What is the role of UNAIDS and WHO in the field of vaccine development?

UNAIDS and WHO joined efforts, creating a WHO-UNAIDS HIV Vaccine Initiative. The joint initiative does not fund trials. Its role is to provide international coordination and to build up the capacity of developing countries to conduct such trials. It also plays a useful role in setting standards. Specifically, the Initiative:

- Advocates for HIV vaccines;
- Helps developing countries prepare to conduct vaccine trials in a scientifically and ethically sound way;
- Promotes and supports the development of HIV vaccines that would be appropriate for use in developing countries;
- Supports the surveillance of different subtypes of HIV-1 in the world, particularly in developing countries;

- Prepares for the availability of, and access to, future HIV vaccines.

The WHO-UNAIDS HIV Vaccine Initiative officially launched the Africa AIDS Vaccine Programme (AAVP) at a Forum conducted in South Africa in June 2002. AAVP is an African Network to facilitate the development and evaluation of HIV vaccines for Africa, through capacity-building and regional and international collaboration.

III/12 What is the Global HIV Vaccine Enterprise?

The Global HIV Vaccine Enterprise is a new alliance of independent organizations around the world dedicated to accelerating the development of a preventive HIV vaccine through implementing a shared scientific plan that spans vaccine discovery, product development and manufacturing, and clinical trials; mobilising significant new funding to achieve the scientific plan; and promoting greater collaboration through efficient, faster ways for researchers to share successes and failures and avoid duplication of efforts. Originally proposed in June 2003 in an article published in the journal *Science* by 24 leaders in HIV vaccine research, the Enterprise represents a new way of doing business. The authors of the *Science* paper argued that while most HIV vaccine research has been conducted by small teams of investigators working independently, the scale of current projects is not sufficient to solve the major scientific challenges facing the field. The Enterprise calls for complementing current investigator-led efforts with large-scale, well-funded, and collaborative efforts across institutions and disciplines. The Enterprise focuses on tackling major scientific problems that have proven too difficult for any one group to address alone. It brings together researchers, funders, and advocates from private industry, academia, government agencies, and non-governmental organizations in developed and developing countries. Participants in the initial development of the Enterprise included the Bill & Melinda Gates Foundation, the French Agence Nationale de Recherches sur le SIDA, the International AIDS Vaccine Initiative, UNAIDS, the U.S. National Institutes of Health, the Wellcome Trust, and the World Health Organization. WHO and UNAIDS are committed to supporting the Enterprise, by contributing to capacity building in developing countries for the conduct of clinical trials at the highest scientific and ethical standards, compiling information on the distribution of different virus sub-types and addressing issues such as future access to HIV vaccines as part of HIV prevention, treatment, care and support programmes. Two recent new commitments by Enterprise partners support elements of the Enterprise Scientific Plan. The first is the NIAID Center for HIV/AIDS Vaccine Immunology (called CHAVI) for US\$14.9 million in 2005 and up to US\$49 million/year subsequently for up to seven years. The second are the Bill and Melinda Gates Foundation three requests for proposals for Consortia/Centres for Vaccine Discovery (Antibodies), Vaccine Discovery (T-Cells) and Vaccine Immune Monitoring totalling US\$360 million over five years.

III/13 What efforts are being made to make an HIV vaccine available once it is produced?

Usually, vaccines arrive in low- and middle-income countries many years after they are introduced in high-income countries. This cannot be allowed to happen in the case of HIV. Effective HIV vaccines need to be made rapidly available and affordable with simultaneous access in both low- and high-income countries. WHO, UNAIDS and the International AIDS Vaccine Initiative (IAVI) have been discussing strategies to ensure the rapid availability of future HIV vaccines. Many of the challenges are similar to those relating to expanding

access to antiretroviral drugs. IAVI and others are proposing significant changes to existing approaches to vaccine production, licensing, pricing, purchasing and distribution.

Differential pricing, together with financial support from donors, will be necessary for low-income countries. Technical assistance and coordination by international agencies and partners will be needed. Since vaccination will not immediately be available to everyone, costs and benefits have to be calculated to determine where the initial focus should be. Policy-makers must also decide what to do if the first available vaccines are only marginally effective or have significant side effects. WHO and UNAIDS, in collaboration with IAVI, conducted an international study to identify potential policies that will guide the introduction and use of future HIV vaccines, and obtained initial information on global and regional needs for future vaccines. This information is essential to industry, public health authorities and financial institutions.

III/14 There seems to be a lack of economic incentive for the private sector to invest in vaccine development. How can this be changed?

In general, preventive vaccines are not as financially lucrative for the pharmaceutical industry as therapeutic products, particularly drugs that patients need to take repeatedly (as in the treatment of chronic disease). This has been a problem with the development of other vaccines in the past. In addition, the costs for development, evaluation, and liability are much higher for vaccines than for most other products. Because of these obstacles, WHO and UNAIDS are encouraging the pharmaceutical industry's work in this area, and are facilitating partnerships—among governments, foundations, research institutions and industry—to share the risks, costs and benefits of vaccine development.

III/15 What additional resources are needed for more rapid vaccine development?

There are two main ways to accelerate the timeline for discovery and development of an AIDS vaccine:

- increase the number of high-quality, viable candidate vaccines entering and moving through the product development pipeline, from Phase I safety studies to Phase III efficacy trials and licensure
- enhance the quality of those candidates and their chances of successfully progressing through the pipeline, through improvements in applied research and in techniques supporting vaccine testing, such as laboratory standards.

To accomplish these, R&D spending needs to rise from the current level of **around \$550 million a year (2002 figures) to approximately \$1.1 billion a year**. Estimates by IAVI, UNAIDS, AVAC (AIDS Vaccine Advocacy Coalition) and the Alliance for Microbicide Development tracking global AIDS vaccine R&D expenditure are that, of the \$550 million spent in the search for an AIDS vaccine in 2002 (see Table below),:

- US \$350 million (64%) went for basic and applied research
- US \$155 million (28%) went for product development
- US \$43 million (8%) went for other activities including building trials capacity in developing countries.

Only a small share of this went to the kind of goal-directed, collaborative work that is now being proposed under the Global HIV Vaccine Enterprise to address the key unanswered scientific questions. In addition to continued support by national health research authorities of a wide range of investigator-initiated basic research leading to better vaccine design,

more efforts and increased resources are needed to address key applied research questions, such as:

- how to elicit broadly neutralizing antibody responses
- prioritizing, developing and testing promising vaccine candidates efficiently in field trials.

Section IV: Microbicides

Microbicides are chemical substances that kill viruses and bacteria when applied vaginally before sexual intercourse. Applied inside the vagina in the form of gel, cream, suppository or film, a microbicide would prevent infection with HIV and, possibly, other sexually transmitted infections. If spermicidal, it might also be used for preventing unintended pregnancy. The ideal product would be odourless and colourless. As such, microbicides could increase the options for women who find it difficult or impossible to persuade their partners to use a condom. Microbicides that could protect during rectal intercourse are under development.

IV/1 Why have microbicides been heralded as a potentially powerful tool in the fight against HIV?

Microbicides offer the best promise of a prevention tool women can control. They could have a substantial impact on the epidemic. Modelling indicates that even a 60%-effective microbicide could have considerable impact on HIV transmission: if used regularly by just 20% of women in countries with substantial epidemics, hundreds of thousands of new infections could be averted over three years.

IV/2 How would microbicides benefit women and others who cannot negotiate safe sex?

As a prevention method that can be self-administered and might be undetectable to partners, microbicides could increase the options for women who find it difficult or impossible to persuade their spouses or other sex partners to use a condom. Acceptability studies in South Africa, Uganda and Zimbabwe suggest that women who seldom or never use condoms would reduce their overall risk of infection if an effective microbicide were available to them at low cost.

IV/3 What is happening with microbicide research?

There are six large efficacy trials underway on five different microbicide products. They include three entry inhibitors, a surfactant (detergent) and an acid buffering agent. Various second generation options are in the pipeline. They include HIV fusion inhibitors – CCR5, gp120 and gp41 blocker, and gels containing antiretroviral medications. Formulations being explored include non-coitally dependent products that could be applied daily or weekly, such as vaginal rings releasing protective levels of antiretroviral drugs, other devices in which the microbicidal drug could be released on contact with semen and genetically modified lactobacilli which would release anti-viral proteins. Products for use rectally are also being explored.

The increased attention to microbicide development from the scientific community, public sector funding agencies and a few biotechnology companies, means that more compounds

are entering Phase II, Phase I and preclinical stages of development. The Gates Foundation has recently provided International Partnership for Microbicides (IPM) with US\$60 million and previously funded the US-based NGO CONRAD with US\$ 25 million to accelerate microbicide development. The International Working Group on Microbicides, which includes public agencies from across the world among its members, continues to promote and facilitate the development of microbicides. It is estimated that an effective product may be available on the world market in 5 to 10 years.

IV/4: An earlier trial on the potential microbicide nonoxynol-9 showed that it increased rather than decreased the risk of HIV infection. How can we be sure that such a result will not happen again with the current products in Phase III clinical testing?

Nonoxynol-9 is a widely available spermicide that was shown to kill HIV in the laboratory. Clinical research on nonoxynol-9 had given conflicting results on whether or not it provided protection against HIV. Since this product was widely available and on the market, it was essential that a clear answer be established. By contrast, none of the products currently in Phase III testing is available in the market, and the trials will only continue if they show positive benefit in prevention of HIV infection among users.

Section V: Condoms and safer sex

Prevention is the first line of defense against AIDS, and the correct and consistent use of condoms is a mainstay of HIV prevention approaches. Condom use to prevent HIV is most effective when it is part of a broader safer sexual behavior package that includes sexual abstinence, non-penetrative sexual practices, and reduced numbers of sexual partners.

But many people, especially young people and young girls, do not have sufficient information about the importance of using condoms, nor are there sufficient supplies of condoms. Cost is also a major issue. UNAIDS continues to make the promotion and availability of condoms, including the female condom, a key priority.

V/1 Why is condom promotion and distribution absolutely essential in limiting the spread of HIV and AIDS?

The vast majority of HIV infections are sexually transmitted. There are only four ways to prevent sexual transmission of HIV. These are: (1) abstinence, (2) monogamous relations with an uninfected partner, (3) non-penetrative sex, and (4) consistent and correct use of male or female condoms. Studies consistently show that in every population above the age of sexual debut there are many people who are either unable or unwilling to practice abstinence, monogamy and non-penetrative sex. This leaves condoms for protecting these people and their partners.

V/2 Are condoms really effective in preventing HIV transmission?

The WHO, UNAIDS & UNFPA Position statement on condoms and HIV prevention states that condom use is a critical element in a comprehensive, effective and sustainable approach to HIV prevention and treatment. Further, it says that the male latex condom is the single, most efficient, available technology to reduce the sexual transmission of HIV and

other sexually transmitted infections. When used properly and consistently, condoms are a proven and effective means for preventing HIV infection in women and men.

Based on research between discordant couples (one HIV-negative and one HIV-positive), condoms have been found to be 90% effective. The vast majority of condom failures result not from leakage or permeability of the latex material, but from improper use, breakage, or slippage.

It is important to emphasize that an effectiveness of 90% for condoms does not mean HIV transmission will take place in 10% of sexual acts in which condoms are used. This means that each time a person has sex using a condom, he or she reduces their risk to acquire HIV by 90%.

V/3 What about other STIs?

The data are less complete for other STIs, but enough evidence exists to make condoms the recommended strategy for preventing gonorrhoea, chlamydia, trichomoniasis, and syphilis. Studies to establish reliably the effectiveness of condoms against specific STIs are difficult to conduct in a scientifically rigorous and ethical manner, but a number of studies are underway and more are planned. Studies have already proven the effectiveness of condoms in preventing gonorrhoea in men.

V/4 Is there any evidence that condom use is effective in reducing HIV infections in generalized epidemics?

More data is now emerging that demonstrates the effectiveness of condoms in preventing HIV transmission in generalized epidemics. A study from South Africa, published in the journal "AIDS", found that when enough young men use condoms consistently, there is a clear protective effect for both the individual and the population at large.

V/5 Can HIV pass through a condom?

Condoms provide an impermeable barrier to viruses and to sperm barrier that indeed blocks the passage of organisms much smaller than HIV. Condoms are required to undergo demanding tests, including tests for holes, before they are distributed or sold. If any holes or perforations are found, the condoms are discarded.

V/6 Don't condoms often "fail" during intercourse?

The evidence from valid studies conducted by reputable and reliable organizations is overwhelmingly that condoms provide effective protection from sexually transmitted HIV infection and other STIs, as well as unwanted pregnancy. Condom "failure" occurs on the rare occasion that a person contracts an infection or becomes pregnant despite the use of a condom. Such "failure" is very infrequent and is usually associated with condom breakage or slippage. Most slippage and breakage of condoms are caused by incorrect use, though there is an increased likelihood of breakage if the condom is past its expiry date or has been exposed to excessive heat. If condoms are to prevent HIV and STIs, they must be used correctly and consistently. Occasional use provides no more than occasional protection.

V/7 Do condoms lead to increased promiscuity?

No, condoms do not lead to increased promiscuity. Since the early 1990s, extensive research has shown that education about sexuality and access to condoms do not lead young people to begin having sex, or to have more partners. In fact, condoms, when distributed with educational materials as part of a comprehensive prevention package, have been shown to significantly lower sexual risk and activity, both among those already sexually active and those who are not.

V/8 What is the “ABC” prevention approach?

Just as combination treatment attacks HIV at different phases of virus replication, combination prevention includes various safer sex behaviour strategies that informed individuals who are in a position to decide for themselves can choose at different times in their lives to reduce their risk of exposing themselves or others to HIV (Global HIV Prevention Working Group, 2003). These are often referred to as the ABCs of combination prevention:

- **A means abstinence**—not engaging in sexual intercourse or delaying sexual initiation. Whether abstinence occurs by delaying sexual debut or by adopting a period of abstinence at a later stage, access to information and education about alternative safer sexual practices is critical to avoid HIV infection when sexual activity begins or is resumed.
- **B means being safer**—by being faithful to one’s partner or reducing the number of sexual partners. The lifetime number of sexual partners is a very important predictor of HIV infection. Thus, having fewer sexual partners reduces the risk of HIV exposure. However, strategies to promote faithfulness among couples do not necessarily lead to lower incidence of HIV unless neither partner has HIV infection and both are consistently faithful.
- **C means correct and consistent condom use**—condoms reduce the risk of HIV transmission for sexually active young people, couples in which one person is HIV-positive, sex workers and their clients, and anyone engaging in sexual activity with partners who may have been at risk of HIV exposure. Research has found that if people do not have access to condoms, other prevention strategies lose much of their potential effectiveness.

A, B, and C interventions can be adapted and combined in a balanced approach that will vary by cultural context, the population addressed and the stage of the epidemic.

V/9 Why does UNAIDS promote condom use if condoms are not fool-proof?

UNAIDS is a strong advocate for condom promotion and distribution because it is a proven fact that condoms can prevent HIV infection during vaginal, anal, or oral sex. And condoms are the only existing products that can do this.

V/10 What is the "condom gap"?

UNFPA estimates that 8 billion condoms were needed in 2000 for HIV/STI prevention alone, and that, by 2015, at least 19 billion condoms will be needed. These figures exclude

condoms needed for family planning purposes, and assume that the condoms would, in any case, not be used consistently.

V/11 What is being done to overcome the condom gap?

Cost is a major issue. Costs will rise from an estimated US\$ 239 million in 2000 to an estimated US\$ 557 million in 2015. This cost does not include delivery, distribution, promotion or other services.

Resources to meet demand for condoms come from domestic government sources and out-of-pocket expenditures; multilateral agencies, including the United Nations Population Fund (UNFPA) and the World Bank Multi-Country AIDS Programme (MAP); the Global Fund to fight AIDS, TB, and Malaria; the private sector (foundations, employers, international nongovernmental organisations) and bilateral donors. Donors provided 3.574 billion condoms in 2002, at a cost of US\$ 94.9 million. Condom funding peaked in 1996 when international funding of condoms was at US\$ 68 million, but it subsequently declined to US\$ 40 million annually in 1999 and 2000.

V/12 Are condoms enough?

No. It is essential that all people, including young people and women and girls, have access to the information, education and life skills that enable them to have safe and responsible sexual relations and negotiate safer sex, including condom use. This is especially important with regard to changing harmful gender norms that make men less likely to use condoms, and make women and girls less able to insist on their use.

V/13 What makes someone use a condom?

Knowledge about HIV and AIDS, easy accessibility and affordability, and social support to do so. Increasing condom accessibility and availability also increases condom use. In Brazil, there was a massive increase in the uptake of condoms when prices came down in the early 1990s. However, almost everywhere, sexually active young people (especially young women) are denied accurate information about condoms. Researchers in Kenya report that 54% of young people do not believe that condoms protect against HIV infection.

V/14 What are the most effective ways for women to protect themselves against HIV infection during sexual intercourse?

Besides mutual fidelity between uninfected partners, correct use of a condom "from start to finish" continues to be the single most effective means for women and men to protect themselves from HIV infection through sexual intercourse. However, because of their social and cultural situations, women are often unable to insist on condom use by their male partners. This should be countered by the promotion of the following:

- Sexual health education, sexual responsibility and gender sensitivity for men/boys;
- Negotiating and life-skills for women/girls;
- Economic, social and political equality for women/girls;
- Promotion and widespread distribution of female condoms;

- Urgent development and distribution of microbicides.

V/15 What has UNAIDS done to promote the female condom?

In 1996, UNAIDS and the sole manufacturer of female condoms established a special discount price of about US\$ 0.60 per condom for use by the public sector and non-profit organizations, especially in developing countries, in order to make the female condom more easily available and affordable. As a strong advocate for the inclusion of female condoms in prevention programmes, UNAIDS, in collaboration with the manufacturer, has also made the female condom available to many developing countries to encourage its integration into existing condom programmes.

Ghana is one of the countries that has a national programme to boost female condom use, including high-level political commitment (notably, by the former First Lady, Nana Konadu Agyeman Rawlings), social marketing, and distribution by both the public and private sectors. Technical assistance to country programmes is also provided by WHO and UNFPA. In addition, UNAIDS has produced and disseminated key documents and Best Practices on the introduction and integration of female condoms in countries, including the recent "The Female Condom: A Guide for Planning and Programming".

Section VI: Religious organizations and the response to AIDS

UNAIDS encourages religious organizations to support effective prevention and care programmes, including the use of condoms as part of these programmes. Many do support such programmes. Though abstinence and monogamy (involving two seronegative partners) do protect against HIV transmission, statistics in every region and age group (after sexual debut) indicate that large numbers of people, including young people, do not practise abstinence or monogamy.

UNAIDS believes it is every person's right, including young people, to have access to effective education on human sexuality, health and life skills to enable that person to make informed choices and follow through on them, including abstinence and monogamy. Research has shown that such education does not result in increased sexual relations.

VI/1 What is UNAIDS' position regarding religious organizations that prohibit the use of condoms?

UNAIDS provides factual, scientific information about condoms, and encourages religious organizations and leaders to support effective prevention and care programmes. UNAIDS encourages the use of condoms as part of these programmes, and encourages religious organizations to debate and consider the use of condoms.

VI/2 How does UNAIDS view abstinence and monogamy?

UNAIDS recognizes that abstinence and monogamy (involving two seronegative partners) protects against HIV transmission. UNAIDS can also provide scientific evidence that a delayed sexual debut is a prevention measure. However, UNAIDS also recognizes that statistics in every region and age group (after sexual debut) indicate that large numbers of people, including young people, do not practise abstinence or monogamy. UNAIDS believes

that it is every person's right, including young people, to have access to effective education regarding human sexuality, health and life skills to enable that person to make informed choices and follow through on them, including abstinence and monogamy. In collaboration with various organizations, UNAIDS advocates that a call for abstinence and monogamy be done in conjunction with education on human sexuality in order for people to be able to practise these approaches successfully. Research has shown that sexual health and life skills education can be a support for abstinence, monogamy and delayed sexual debut. Many religious organizations provide such education.

VI/3 What have religious organizations done in the field of AIDS so far?

Religious organizations have for two decades cared for people living with HIV in various ways, both at hospitals and in the communities. Religious organizations are also part of coping mechanisms in hard-hit communities.

VI/4 Does UNAIDS collaborate with religious organizations that are proselytizing?

UNAIDS works with all organizations that have sound HIV policies and that perform effective and ethical work in the field of AIDS.

VI/5 What is the most important work religious organizations can do to fight AIDS?

Battling stigma and discrimination against people living with HIV, helping communities eradicate such stigma and discrimination, and mobilizing communities in HIV prevention and care efforts. They can also de-emphasize labelling or blaming that lead to stigma and discrimination, and emphasize openness, acceptance, reconciliation, compassion and action: within individuals, between individuals, within communities and between communities.

VI/6 What can UNAIDS do to facilitate the work of religious organizations?

UNAIDS can broker partnerships with religious organizations and facilitate collaboration with governments and AIDS service organizations at all levels. UNAIDS can also give technical input to religious organizations as they create their action plans and strategies on AIDS.

Section VII: Mother-to-Child Transmission

The internationally agreed approach to preventing MTCT includes: (1) primary prevention of HIV among prospective parents; (2) prevention of unwanted pregnancies among HIV-positive women; (3) prevention of transmission of HIV from mother to child; and (4) the care and treatment of HIV-positive mothers in the context of mother-to-child transmission.

Reduction in prices of antiretrovirals (ARVs), simpler regimens, donations of ARVs, and increased commitment and funding for the prevention of MTCT provide the potential for significant expansion of these services, although the global coverage of PMTCT is still low, below 10%.

As to infant feeding, an HIV-positive woman, including women on ART, should be counseled on infant feeding and be allowed to choose the option most feasible and safe in her

circumstances. If it is not feasible, affordable, sustainable, and safe to feed with suitable infant formula, HIV-positive women should be counseled to practice exclusive breastfeeding for the first few months of the infant's life and to discontinue breastfeeding when an alternative form of feeding becomes feasible

VII/1 What can be done to prevent babies from acquiring HIV from their infected mothers?

A three-fold strategy is needed in order to prevent MTCT:

- Preventing women and girls of child-bearing age, and those lactating, from acquiring HIV infection;
- Avoiding unwanted pregnancies among HIV-positive women;
- Preventing the transmission of HIV from an HIV-positive mother to her infant during pregnancy, labour, delivery, and breastfeeding, by providing VCT, ARV therapy, safe delivery practices, infant feeding counseling, and where indicated, breast milk substitutes.

VII/2 What are the antiretroviral drugs used to prevent mother-to-child transmission and how do they work?

A number of regimens, long-term and short-term, involving zidovudine alone, zidovudine and lamivudine, and nevirapine, help to prevent MTCT by decreasing viral load in the mother and through prophylaxis in the infant during and after exposure to the virus.

VII/3 Do antiretroviral drugs also prevent MTCT during breastfeeding?

Not totally. Studies conducted in breastfeeding populations have shown that the protective efficacy of the various drug regimens is diminished when babies continue to be exposed to HIV through breastfeeding. In one such study (the PETRA study), the reduction in transmission seen at 6 weeks was no longer significant at 18 months of age. This underlines the substantial risk of HIV transmission during breastfeeding which can greatly erode the short-term benefit of drugs to prevent MTCT of HIV, and the urgent need for research to improve the safety of breastfeeding for infants born to HIV-positive women. Potential strategies include modifications to the pattern and duration of breastfeeding with an emphasis on exclusive breastfeeding, ARV treatment for breastfeeding mothers, prevention treatment for the baby continued through the period of breastfeeding, or a combination of these.

VII/4 What effect do short-course regimens of antiretroviral have on the mother and infant?

The safety of preventive treatments, including zidovudine alone, zidovudine and lamivudine, and nevirapine, has been studied extensively for both breastfeeding and non-breastfeeding populations worldwide. Information currently available does not suggest any adverse effects on the health of the mother, growth and development of infants, or the health and mortality of infants infected despite prophylaxis. The only possible risk for the mother is anaemia. However, pregnant women taking ARVs for HIV will be doing so under the supervision of the

maternal health services, where screening for anaemia (and treatment, if necessary) should be routine procedures.

While resistant virus may develop quickly to antiretroviral drug regimens that do not fully suppress viral replication (such as those including lamivudine and nevirapine), evidence indicates that virus containing drug-resistant mutations decreases once the antiretroviral drugs are discontinued. Mutant virus may remain present in an individual in very low levels, which could reduce the effectiveness of future antiretroviral treatment for the mother.

VII/5 Are ARV drugs enough for successful prevention of MTCT?

No. The prevention of MTCT involves more than the provision of antiretroviral drugs. Voluntary counseling and testing are an essential part of any prevention of MTCT strategy, because VCT provides: (1) prevention information and support in order to avoid infection for childbearing women not infected; and (2) the knowledge of one's status, and referral so that positive women can access prevention of MTCT interventions. During prevention of MTCT regimens, there is further need for appropriate counseling and testing services, as well as support for mothers and infants in the taking of ARVs and on infant feeding options. Moreover, providing care and treatment for the HIV-positive mothers is not only ethically required, but also provides an incentive to access HIV prevention, care and VCT for themselves, their partners and families.

VII/6 How feasible is it to provide ARV drugs for MTCT in low-income countries?

The feasibility of providing ARVs to prevent MTCT has been increasing since 1994 when a long-course regimen using zidovudine was shown to reduce MTCT by about two-thirds in the absence of breastfeeding. At an average cost of US\$ 1000 per pregnancy, this regimen was seen as very expensive for use in poor countries. In early 1998, studies in Thailand showed that a relatively simple drug regimen, a short one-month course of zidovudine (AZT) given to HIV-infected mothers late in pregnancy, could halve the rate of HIV transmission to their infants as long as the women also avoided breastfeeding. In Côte d'Ivoire and Burkina Faso, it was shown that, even if the women breastfed their infants, the rate of MTCT was still cut by a third. Most significantly, a 1999 study in Uganda showed that one dose of nevirapine to the mother at the onset of labour followed by another dose given to the infant after delivery was highly effective in reducing MTCT. Further studies have shown this nevirapine regimen to be safe as well. The regimen is easy to take because it comprises a total of two doses and costs about US\$ 4. Other short-course regimens involving zidovudine, and a combination of zidovudine and another drug called lamivudine (the PETRA study), have also been shown to be effective.

VII/7 What is recommended regarding breastfeeding by HIV-positive mothers?

Up to 20% of infants born to HIV-positive mothers may acquire HIV through breastfeeding. But the alternative to breastfeeding, the use of infant formula, is problematic. First, it poses risks because it means the baby is not receiving the special vitamins, nutrients and protective agents found in breast milk. Secondly the use of infant formula may not be feasible or safe. The cost of infant formula often puts it beyond the reach of poor families in developing countries, even when the products are widely available. Many women also lack access to the knowledge, potable water and fuel needed to prepare replacement feeds

safely, or simply have no time to prepare them. If used incorrectly - mixed with unsafe water, for example, or over-diluted - a breast milk substitute can cause infections, malnutrition and even death. Furthermore, if a mother chooses not to breastfeed in settings where breastfeeding is the norm, this may draw attention to her HIV status and invite discrimination, violence or abandonment by her family and community. A further factor to be considered is that a mother who does not breastfeed loses the natural contraceptive effect of the practice and is at increased risk of becoming pregnant soon after having given birth.

Given these dilemmas, recent consultations held by the UN Interagency Task Team concluded that an HIV-positive mother should be counseled on the risks and benefits of different infant feeding options and should be guided in selecting the most suitable option for her situation. The ideal option is the one that is most acceptable, feasible, affordable, sustainable and safe in her particular context. If one of these conditions is not met with regard to formula feeding, the woman should be counseled to practice exclusive breastfeeding for the first few months. The final decision should be the woman's, and she should be supported in her choice.

For HIV-positive women who choose to breastfeed, exclusive breastfeeding (as opposed to "mixed feeding"-breastfeeding mixed with bottle feeding of water or formula, or providing other foods) is recommended for the first months of an infant's life, and should be discontinued once an alternative form of feeding becomes feasible. This is because mixed feeding may increase the risk of HIV infection. Indirect evidence suggests that keeping the period of transition from exclusive breastfeeding to alternative feeding as short as possible may reduce that risk. Unfortunately, the best duration for this is not yet known and may vary according to the infant's age and/or the environment.

Section VIII: HIV Testing

VIII/1 What are the benefits of HIV Testing?

Knowledge of HIV status is the gateway to AIDS treatment and has documented prevention benefits; however, the current reach of HIV testing services is poor and uptake is often low, largely because of fear of stigma and discrimination. The cornerstones of HIV testing scale-up include strengthened protection from stigma and discrimination as well as assured access to integrated prevention, treatment and care services. Public health strategies to increase knowledge of HIV status and human rights protection are mutually reinforcing and should be integrated for greatest effect in reducing HIV transmission and improving the quality of life of people living with HIV.

VIII/2 What is UNAIDS' position on HIV Testing?

UNAIDS promotes expanded access to both client-initiated and provider-initiated voluntary, confidential HIV testing, conducted with informed consent and accompanied by counselling for both HIV-positive and HIV-negative individuals. With respect to provider-initiated testing, in all settings, individuals retain the right to refuse testing, i.e. to 'opt out' of a routine offer of testing. All testing needs to be accompanied by referral to medical and psychosocial services for those who receive a positive test result and by community education and legal and policy reform to counter stigma and discrimination. [UNAIDS policy statement on HIV testing](#).

Section IX: Care, Treatment and Support

Vastly increased access to comprehensive HIV care and support, including ARVs and treatment for HIV-related opportunistic infections, is a global priority. More affordable medicines will catalyze strengthened health care delivery systems. Better health care delivery systems will provide greater capacity to deliver affordable medical technology.

UNAIDS and its Cosponsors are working closely with governments, civil society, people living with HIV and the pharmaceutical industry, to expand dramatically the provision of HIV-related treatment in resource-poor settings. WHO has declared that lack of HIV treatment in developing countries is a global public health emergency.

IX/1 What is the current status of HIV therapy?

The use of ARVs in combinations of three or more drugs has dramatically reduced AIDS-related morbidity and mortality since 1996 in countries where they are widely accessible. While not a cure for AIDS, combination ARV therapy has enabled HIV-positive people to live longer, healthier, more productive lives by reducing viremia (the amount of HIV in the blood) and increasing the number of CD4+ cells (white blood cells that are central to the effective functioning of the immune system).

ARV treatment regimens must be adhered to closely. Dosing requirements, number of pills per dose, and dietary restrictions are some of the factors that may inhibit an individual's ability to take these medications regularly and as prescribed. Failure to maintain adherence can result in treatment failure and the emergence of drug-resistant HIV. Short-term toxicities, such as nausea, diarrhoea, central nervous system side effects and rash, must be closely monitored during the early stages of treatment. Long-term complications, such as body shape changes, elevations in blood lipids, peripheral neuropathy, diabetes, and kidney and liver function abnormalities may also occur.

Until recently, the high cost of the medicines, inadequate health care infrastructure and lack of financing has prevented wide use of combination ARV treatment in low- and middle-income countries. However, increased political and economic commitment in recent years, stimulated by people living with HIV, civil society and other partners, has opened the scope for dramatic expansion of access to HIV therapy.

Twelve ARV medicines have been included in the WHO Essential Medicines List following careful analysis of current evidence of ARV efficacy in developing countries which shows that these medicines can be used effectively and safely in poor settings. The long-sought inclusion of ARVs in WHO's Essential Medicines List will encourage governments in hard-hit countries to further expand the distribution of these vital drugs to those who need them.

IX/2 How many people are receiving ARV therapy?

As of December 2005, an estimated 1.3 million people living in low and middle-income countries had access to ARV therapy.

Table 1. Estimated number of people receiving ARV therapy, people needing ARV therapy, and percentage coverage in low- and middle-income countries according to region, December 2005

Geographical region	Estimated no. of people receiving ARV therapy, December 2005	Estimated no. of people needing ARV therapy, December 2005	ARV therapy coverage, December 2005
Sub-Saharan Africa	810,000	4,700,000	17%
Latin America & Caribbean	315,000	465,000	68%
East, South & South East Asia	180,000	1,100,000	16%
Europe and Central Asia	21,000	160,000	13%
Middle East & North Africa	4,000	75,000	5%
Total	1,330,000	6.5 million	20%

IX/3 What are the barriers to increased access to HIV-related treatments in low- and middle-income countries?

The primary barriers to increased access to ARV therapy and treatments for HIV-related opportunistic infections are high costs, lack of sufficient financing, weak health infrastructures, lack of diagnostics and monitoring equipment, and insufficient numbers and inappropriate distribution of trained health care providers.

IX/4 Are the UNAIDS Secretariat and Cosponsors working with generic companies?

Yes, they are. WHO and the UNAIDS Secretariat promote the engagement of both generic and research-based pharmaceutical companies in the response to AIDS. WHO and UNAIDS co-hosted meetings in 2002 and 2003 with chief and senior executives of key generic manufacturers of HIV-related medicines to engage the generic pharmaceutical industry more intensively in the response to the epidemic. A number of generic companies, in addition to research and development-based pharmaceuticals, have submitted applications and have been reviewed by the quality assessment project (known as "pre-qualification") undertaken by WHO, with support from UNICEF and the UNAIDS Secretariat. Products from both branded and generic manufacturers have met the international standards used by WHO in its "prequalification" exercise (the results of the quality assessments are available at: http://www.who.int/vaccines-access/quality/un_prequalified/prequalification_system.htm)

Generic drugs, diagnostics and other commodities have also been included in the published mapping of sources and prices of HIV-related medications undertaken by WHO, UNICEF, Médecins Sans Frontières and the UNAIDS Secretariat. Representatives of the generic pharmaceutical industry, along with research-based companies, have participated in the Contact Group on Accelerating Access to AIDS-related care.

IX/5 What is UNAIDS's position regarding the exporting of generic drugs (including ARVs)?

UNAIDS supports the engagement of a broad range of partners in the response to the AIDS epidemic. Large volumes of antiretroviral medicines will be required to scale up access to treatment, and both research-based and generic manufacturers must be engaged. For this reason, UNAIDS welcomes the legislative reforms taking place in Canada to allow that country's generic suppliers to export HIV medicines to developing countries that do not have their own manufacturing capacity. UNAIDS also supports generic competition as one way of reducing the cost of HIV-related medicines and of increasing access to HIV care and treatment.

The *Declaration of Commitment* unanimously endorsed by Member States at the UN General Assembly Special Session on HIV/AIDS emphasizes the importance of cooperation in strengthening pharmaceutical policies and practices, including those applicable to generic drugs. The WHO *Medicines Strategy* includes promotion of generic competition.

IX/6 Does UNAIDS support FDC's (Fixed Drug Combinations)?

Yes. Triple combination antiretroviral therapy has long been the standard for treating HIV infection. The pharmaceutical industry is contributing to simplifying treatment regimens through developing and manufacturing fixed-dose combination formulations. Fixed-dose combinations permit all three individual molecules to be taken in one tablet, capsule or, in the future, a solution which is of special importance to children.

Three fixed-dose combinations, one each from Indian generics producers Cipla and Ranbaxy, and one from GlaxoSmithKline, have been approved by the WHO pre-qualification quality assessment programme. The generic fixed-dose combinations provide a WHO recommended, first-line regimen. Patents for individual components are often held by different originator companies, and the research-based industry is exploring multi-company arrangements to allow their products under patent to be combined or packaged together in blister packs. Fixed-dose combination antiretrovirals offer a number of possible advantages. They can:

- increase patient adherence to treatment;
- delay the development of resistance;
- lower the total cost, including production, storage, transport, dispensing and other health system costs;
- reduce the risk of medication errors by prescribers, dispensers and patients themselves;
- simplify supply-system functioning and increase security; and
- facilitate patient counselling and education, and reduce waiting time for patients.

IX/7 Which countries are now offering universal coverage for ARV treatment?

Many countries, including those with high HIV prevalence or with emerging epidemics in large populations, have already been mobilizing in response to the HIV treatment gap. Several countries in Latin America and the Caribbean now offer universal coverage for antiretroviral treatment, including Argentina, Barbados, Chile, Costa Rica, Cuba, Mexico and Uruguay. Bahamas and Guyana are advancing towards universal access. Brazil is engaged in a South-South cooperation programme with Bolivia and Paraguay to achieve universal

access in those countries. Other countries that have made substantial progress include Botswana and Senegal. However, Brazil remains the only country with a large population to achieve universal access to HIV treatment.

IX/8 What is UNAIDS's position regarding the decisions of some pharmaceutical companies to relax certain drug patents in some regions of the world?

Decisions by some research-based pharmaceutical companies not to enforce their patent rights in some regions of the world should be commended as an example of the kind of flexibility that could foster greater access to affordable HIV medicines through imports and local production of less expensive medicines. Voluntary licensing is another traditional mechanism that can contribute to greater affordability of medicines of importance to people living with HIV.

IX/9 Why is it important to ensure the continuation of major research and development of HIV-related medicines?

Innovation of new and improved HIV-related treatments, diagnostics and monitoring technology is essential to the fight against AIDS. Currently available treatments are not a cure, and drug resistance is a threat to continued success with these treatments. Continuing development of simplified treatment regimens, as well as medicines with fewer instances of side effects, will improve patient adherence to the regimens and, in turn, reduce the development of drug resistance. In sub-Saharan Africa, many more countries say they intend to set up their own production facilities. These include Ethiopia, Kenya, Mozambique, Nigeria, Tanzania, Uganda and Zambia. South Africa already launched its first antiretroviral drug in August 2003. All have plans to start manufacturing generics some-time during 2004–2005 (Dummett, 2003).

IX/10 What is being done to facilitate technology transfer between low- and middle-income countries and to control the quality of drugs?

UNAIDS encourages 'South-to-South' cooperation to expand drug access. In October 2002, WHO and the UNAIDS Secretariat brought together generic manufacturers of HIV-related medicines based primarily in developing countries to exchange lessons and views on how they can contribute further to expanding access to these medicines in low- and middle-income countries. In April 2001, India and South Africa signed a declaration of intent to cooperate in a variety of health fields, including technology transfer and import of drugs. Thailand, with considerable experience in generics production, has signed a similar agreement with Ghana. Brazil also has supported technology transfers to other developing countries.

IX/11 What is UNAIDS' position on intellectual property and compulsory licensing?

The UNAIDS Secretariat acknowledges that patents may be considered as an incentive for innovative research and development of new AIDS drugs and, hopefully, the discovery of HIV vaccines. In the absence of a cure and/or a vaccine, and in view of the serious risk of resistance to existing ARV therapies, innovation is crucial.

At the same time, intellectual property rights must be considered in the context of other social interests, such as the human right to health. Patents provide an exclusive right over the protected product, which can impede affordability and access to medicines for people living with HIV in resource-limited countries or otherwise without the means to pay.

In 2001, UNAIDS called for a 'new deal' with industry to ensure that new forms of HIV treatment are made available on a far greater scale to HIV-positive people in low- and middle-income countries as to those in high-income countries. This requires multiple approaches, including differential pricing, regional procurement to secure price-reductions through large-volume purchases, licensing agreements between patent-holding companies and manufacturers in resource-limited countries, reinforcement of health safeguards in trade agreements (including compulsory licensing), and new private and public funding mechanisms to help pay for treatment and other health related commodities in poor countries.

IX/12 What is UNAIDS' position on international trade rules, compulsory licensing and access to HIV medicines?

- International trade agreements and policies can affect access to goods and services that are crucial to HIV prevention, care and impact mitigation. These goods and services include condoms (male and female), AIDS drugs and other pharmaceutical products (such as HIV testing equipment, materials and services), and products and services to ensure the safety of blood transfusions. The most important international trade agreement concerning access to HIV-related medicines and products is the Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS Agreement). While setting out minimum norms (e.g., 20-year patent term) with which WTO members must comply, the TRIPS Agreement provides governments with a number of flexibilities (e.g., compulsory licensing) to protect the public health of their citizens and improve access to affordable medicines. The Doha Declaration of 2001 clarified that “the TRIPS Agreement can and should be interpreted in a manner supportive of WTO members' right to protect public health and, in particular, to promote access to medicines for all”.

IX/13 What are some of the approaches countries are using to help fund access to care and treatment?

A number of different approaches are being used to help fund access to care and treatment in low- and middle-income countries. These include universal, free-of-charge access to treatment programmes through the public sector (the approach used by Brazil and a number of other Latin American countries), direct government subsidies to patients (the approach used by Chile, Côte d'Ivoire, Gabon, Mali, Romania, Senegal and Trinidad and Tobago), and out-of-pocket purchasing by patients after large-volume purchases at reduced prices by governments (the approach being used by Uganda). It is clear, however, that the vast majority of people living with HIV and in need of treatment will not be able to afford to cover the costs of their care. Countries that have maximised treatment access have done so through universal access. In the Brazilian model, for example, HIV treatment is free. HIV care will need to be provided at a price that is proportionate to local purchasing power – and for many people, in many communities, in many countries, that means HIV care and treatment must be free.

IX/14 Why is psychosocial support so essential to effective care, treatment and support?

Counselling, spiritual support, support for disclosing one's HIV-positive status and for engaging in safer sex and safer injecting drug use, end-of-life and bereavement support, peer support, and practical economic assistance are all part of psychosocial support for people living with HIV. Psychosocial support helps to mitigate the devastating impact of AIDS on people's lives.

Psychosocial support is also essential to the success of ARV treatment. A number of studies have shown that psychological problems, such as depression, reduce people's ability to adhere to complex ARV regimens.

IX/15 Why is improved nutrition essential to effective care, treatment and support?

For much of the world's population living with HIV, the need for food remains an overwhelming priority. People living with HIV need substantial nutritional inputs (up to 50% more protein) to fortify their compromised immune systems. Those suffering from hunger, famine and/or nutritional deficits are more likely to fall ill with opportunistic infections and less likely to be able to recover from them. Malnutrition is also one of the major clinical manifestations of HIV disease. Where drought conditions exist, access to clean water is reduced, further increasing the risk of infection for adults, children and infants, particularly those on formula feeding. Clean water supplies and adequate food must be part of an overall HIV treatment, care and support package.

The World Health Organization has prepared guidelines for incorporating nutrition into prevention, care and treatment activities. World Health Assembly resolution WHA57.14 passed in 2005 *"urged Member States, as a matter of priority, to pursue policies and practices that promote, inter alia, the integration of nutrition into a comprehensive response to HIV/AIDS"*.

The implications of HIV and AIDS are increasingly being mainstreamed into policy and programs of a range of development actors, including governments. In addition to nutrition support for individuals on treatment, interventions increasingly respond to the important links to household food security, and the need to support livelihoods at a time when they may be most threatened.

IX/16 What is the role of traditional healers and pharmacists in HIV care, support and treatment?

Many people in resource-limited settings rely on traditional healers or pharmacists for their health care needs. Effective partnerships between formal health care systems and traditional healers and pharmacists have been shown to significantly improve HIV treatment, care and support. Collaboration with and education of traditional healers can also help dispel the many myths that prevail about the causes of HIV, as well as counter spurious claims about "miracle AIDS cures".

Section X: Resources

X/1 How much is needed for HIV prevention and care programmes in low- and middle-income countries?

Newly revised estimates for effective prevention and care programmes in low- and middle-income countries indicate that US\$ 14.9 billion will be needed in 2006. Financial resource needs will continue to increase significantly so that by 2008 some US\$ 22 billion a year will be needed to successfully combat AIDS, including around US\$ 11.4 billion for prevention, US\$ 5.3 billion for care and treatment, US\$ 2.7 billion for orphan support and US\$ 1.8 billion for programme costs and 0.9% for human resources. For treatment and care, about 55% of these resources will be needed in sub-Saharan Africa, 20% in Asia and the Pacific, 17% in Latin America and the Caribbean, 7% in Eastern Europe and 1% in North Africa and the Near East.

It is estimated that US\$ 6.1 billion was available for AIDS activities from all sources in 2004. In 2005, US\$8.3 billion (range between US\$7.5 and US\$8.5 billion) was available for AIDS activities from all sources. For 2006, and 2007, projections have been made, based on past trends and currently known pledges and commitments that amount to US\$ 8.9 billion and US\$10 billion respectively. It appears that there is a funding gap between resources available and those needed of at least US\$18 billion from 2005 to 2007. However, this is likely to be a significant underestimate. Determining the gap between resources available and resource needed is not a matter of simple subtraction since the resources available might not be follow the exact same pattern as the resource needs estimation.

X/2 How were these figures of future needs calculated?

These figures have been developed using the latest available information and with the invaluable input the Resource Needs Steering Committee and Technical Working Group which are made up of international economists and AIDS experts from donor and developing countries, civil society, United Nations agencies and other international organizations.

Based on real information from countries about the costs of specific programmes, an overall funding amount is calculated in order to achieve a specified coverage of services - how many people will actually get the service. What is new about these estimates, is that they not only cover the costs of delivering a prevention or treatment intervention, they also include the costs of hiring new health and prevention staff, refurbishing existing clinics and hospital, and building new ones.

UNAIDS has been producing resource needs estimates since 2001. Since that time there has been increased access to relevant data, a continuous improvement in the methodologies and new thinking about what comprises a comprehensive package of interventions to turn back the epidemic. Acknowledging that the estimation process has intrinsic limitations, at present these constitute the best available assessment of global needs for AIDS and a rational basis for further discussion about AIDS funding in the international arena.

X/3 Do these estimates include every aspect of a successful AIDS response?

These latest resource needs estimates are based on improved costing data from countries, expand the coverage of services and include selected investments in increasing human resources (primarily physicians and nurses), providing incentives to recruit and retain staff, refurbishing hospitals and health centres and building new health centres.

These estimates do not include the costs of all health care providers needed for a comprehensive treatment and care package, such as nurse practitioners, clinical officers, counsellors, laboratory technicians, and adherence supporters. These estimates provide only limited coverage for universal precautions and support for orphans outside of sub-Saharan Africa. These estimates do not include the costs of vulnerability reduction, such as keeping young people in school, improving the status of women, and combating poverty.

X/4 How much is being spent on AIDS in high-income countries?

UNAIDS does not yet have sufficient information on AIDS expenditure in high-income countries. Data are available for HIV official development assistance from Development Assistance Countries (DAC), multilateral institutions, international NGOs and foundations for the benefit of low- and middle-income countries. Data are also available for in-country AIDS expenditure by governments and national NGOs in low- and middle-income countries.

X/5 The Global Fund to Fight AIDS, Tuberculosis and Malaria

The Global Fund to Fight AIDS, TB and Malaria is a new financing channel established in 2002 as a public-private partnership. Its aim is to rapidly mobilize significant additional resources from donors for the fight against the three diseases in developing countries. The Fund mobilizes and disburses funds to governments, communities, and NGOs. Details of the purpose, scope, and operations of the Fund, as well as the principles underlying its operation, are set out in a Framework Document available on the Global Fund's website at <http://www.theglobalfund.org/en/>. The website also maintains up-to-date information on the status of proposals submitted for funding.

X/6 What is UNAIDS' role in the Global Fund?

The mission of UNAIDS is to lead, strengthen and support an expanded response to the AIDS pandemic aimed at HIV prevention, care and support, reduced vulnerability, and impact alleviation. The Global Fund complements the work of UNAIDS by providing financial resources to strengthen the AIDS response.

In its role as the leading advocate for worldwide action against AIDS, UNAIDS is a principal partner in countries' efforts to access the Global Fund's resources.

UNAIDS is the key provider of strategic leadership, knowledge, policy advice and technical expertise on AIDS to the Global Fund. It makes use of its extensive network of partners to strengthen national capacity and expand civil society and community participation in the response to AIDS. It provides country-level support to the Global Fund, especially to the Country Coordination Mechanisms, through its ten Cosponsors and other partners. UNAIDS

and the Global Fund have developed a Memorandum of Understanding in order to strengthen their partnership.

The UN system has provided support for the Fund since its inception. In April 2001, at the summit in Abuja of the then Organization for African Unity, the UN Secretary-General called for a Global Fund to Fight AIDS, TB and Malaria. Soon after, in June 2001, world leaders unanimously endorsed the concept of the Fund at the UN General Assembly Special Session on HIV/AIDS. Although the Fund does not fall under the UN umbrella, it works closely with the UN and all its partners. The UN Secretary-General, Kofi Annan, is the Patron of the Fund.

X/7 How much funding has the Global Fund allocated to AIDS? What proportion for scaling up access to treatment?

As of September 2005, the total amount allocated by the Global Fund for grants targeting HIV/AIDS stand as follows: US\$ 2.3 billion worth of grant funding has been approved for the first two years of grants (Phase 1), and US\$5.3 billion total over five years (phases 1 and 2).

AIDS accounts for 54 percent of Global Fund resource distribution after five rounds of grants, compared with 29 percent for malaria, 16 percent for tuberculosis, and 1 percent approved for a new category of grants targeting Health Systems Strengthening (HSS). Forty-nine percent of grant expenditures have been allocated for procurement of drugs and commodities.

Over five years, 1.85 million people are projected to receive antiretroviral treatment, 62 million people will be provided with voluntary counseling and testing according to current projections. As of August 2005, 220,000 people had been placed on ARVs through Global Fund grants, and grants targeting AIDS had been approved in 96 countries.

X/8 The Multi-Country HIV/AIDS Program for Africa

The Multi-Country HIV/AIDS Program (MAP) for Africa came into effect in 2001 and is managed by the World Bank. It involves large, zero-interest loans that are largely channelled as grants to communities and civil society with an emphasis on increasing access to HIV prevention, care, and support, and mitigating the impact of the epidemic. It supports country programmes, as well as sub-regional and cross-border initiatives.

X/9 What is the Multi-Country HIV/AIDS Program (MAP) for Africa?

Managed by the World Bank, the Multi-Country HIV/AIDS Program for Africa was launched in September 2000. MAP made an initial amount of US\$500 million, in flexible and rapid funding, available to African countries to assist in scaling up national AIDS efforts. The Bank approved an additional US\$500 million in IDA financing in 2002 for the second stage of the MAP. A similar MAP 'umbrella program', the Multi-Country HIV/AIDS Prevention and Control Adaptable Lending Program (APL) for the Caribbean Region, committing US\$155 million, was approved in June 2001.

The MAP makes funding available to African countries to assist in scaling up national AIDS efforts. The funds are committed to individual AIDS projects developed by countries, using standard IDA credit agreements. MAP funds are available to any African country that meets simple eligibility criteria (including eligibility for IDA credits):

- Satisfactory evidence of a strategic approach to AIDS, developed in a participatory way;
- Establishment of a high-level AIDS coordinating body, with broad representation of key stakeholders from all sectors, including people living with HIV;
- Government commitment to quick implementation arrangements, including channelling grant funds for AIDS activities directly to communities, civil society, and the private sector; and
- Agreement by the government to use multiple implementation agencies, especially community-based and nongovernmental organizations (CBOs/NGOs).

The overall development objective of the MAP is to dramatically increase access to HIV prevention, care, and treatment programmes, with emphasis on vulnerable groups (such as youth, women of childbearing age, and other groups at high risk). The specific development objectives of each individual country project, as stated in the national strategic plans, will provide the basis for this programme and be agreed upon at the time of appraisal of the national projects. A key feature of the MAP is direct support to community organizations, NGOs, and the private sector for local AIDS initiatives.

X/10 How has it been implemented so far?

The World Bank has approved US\$ 1 billion in grants or interest-free loans to support AIDS programmes in sub-Saharan Africa.

In the Caribbean, the Bank has started a similar initiative in which US\$ 155 million will be disbursed in the form of five-year loans. By January 2004, more than US\$ 85 million had been committed to five countries, of which nearly US\$ 10.5 million had been disbursed (World Bank, 2003). In 2003, the World Bank approved a US \$100 million loan to Brazil for responding to AIDS and sexually transmitted infections, bringing the Bank's commitment to Brazil's epidemic to US\$ 430 million.

By January 2004, US\$ 822.3 million had been committed to 24 countries in the region; US\$ 170.6 million had been disbursed. The Programme has committed a further US\$ 16.6 million to sub-regional and cross-border projects.