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I A P A C

M O N T H L Y

Scaling Up Antiretroviral
Therapy in Resource-
Limited Settings:
Guidelines for a Public
Health Approach

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Drugs and
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COVER STORY

Scaling Up Antiretroviral Therapy in Resource-Limited Settings: Guidelines for a Public Health Approach— Executive Summary

In April 2002, the World Health Organization (WHO) released a set of draft guidelines meant to facilitate the expanded use of antiretroviral therapies in resource-limited settings of the developing world. This month's *IAPAC Monthly* features the Executive Summary of "Scaling Up Antiretroviral Therapy in Resource-Limited Settings: Guidelines for a Public Health Approach."



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Rising to the challenge

José M. Zuniga

We have witnessed many medical and public health milestones during the 20-plus year history of the global HIV/AIDS pandemic, the most recent of which is the commitment by international donor countries of US\$2 billion to combat HIV/AIDS, tuberculosis, and malaria worldwide. The establishment of the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM) is a monumental step toward adequately funding the battle against these endemic diseases in resource-limited settings. The International Association of Physicians in AIDS Care (IAPAC) thus applauds both the effort, and the principled action through which the GFATM was so quickly brought to bear after its first call for proposals earlier this year.

Despite general excitement that a commitment of these proportions has finally been manifest, my enthusiasm was tempered by the first disbursement of funds—the potential sum of US\$616 million over the next two years, and US\$1.6 billion over five years. Specifically, I am concerned about funding announced April 25, 2002, for HIV/AIDS programs at country level, of which the overwhelming majority focus primarily, if not exclusively, on HIV/AIDS prevention interventions. There is, in fact, a glaring imbalance.

According to advocacy groups such as Health GAP, as a result of the first round of funding, GFATM-awarded resources in this first round of funding will not even reach half of the countries hardest hit by HIV/AIDS, malaria, and/or tuberculosis. In addition, the few accepted proposals that included HIV/AIDS treatment access will result in treatment for no more than 40,000 people, out of the 10 million people worldwide who are in need of immediate treatment. Sadly, it appears the HIV/AIDS



care agenda has been relegated to a patchy back seat in favor of one focusing almost exclusively upon prevention. This imbalance is something that we can ill-afford to accept in future funding rounds.

While one would be hard pressed to find an individual who would disagree with the merits of and need for enhanced HIV prevention interventions, care for and treatment of those living with HIV/AIDS is both a moral and public health imperative. When we direct our attention to sub-Saharan Africa, for example, where only 0.1 percent of persons living with HIV/AIDS have access to drug treatment, it becomes clear that the veritable death sentence invoked against this mass of human beings through the absence of treatment options, constitutes a human rights abuse for which we share collective responsibility. True commitment to combating HIV/AIDS, therefore, must come not only through money, but by means of funds judiciously spent in a collective push to help governments scale up multi-sectoral national HIV/AIDS strategies,

including care and treatment programs.

Yet, the GFATM's administrators remain largely powerless to provide the balanced funding that much of the international community is calling for, where the tacit policy of donor countries has continually defended the *status quo* of prioritizing prevention programs. Activists contend, and IAPAC agrees, that it is time to redress the decades-long pattern of donor countries discouraging countries from developing treatment programs and refusing to include treatment as part of bilateral programs. Of note, GFATM ambitions were significantly scaled back by donor countries during this first round of proposals. Several developing countries reported external pressure by donor countries to scale down their requests. The *Financial Times* reported a case, for instance, where the government of Malawi was pressured to decrease the scope and amount of funding requested in their proposal. This is not genuine global partnership.

If those tasked with distribution of the GFATM are to be successful in this regard, and moreover, if these funds are to have a meaningful impact upon the pandemic, then clear signals must come from donor countries that a balanced crop of prevention and treatment interventions is in order. To the extent that this has not occurred, and to which the GFATM's Board of Directors has been forced to operate under the cloud of tacit and explicit donor country pressure, the probability of such an impact remains doubtful.

If the HIV/AIDS pandemic as it affects the entire world is truly to be overcome, then those countries most affected by this plague must be empowered to take ownership of national programming. Of particular importance is the need for greater attention

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Access to HIV/AIDS Drugs and Diagnostics of Acceptable Quality

Pilot Procurement, Quality, and Sourcing Project

Suppliers whose HIV-related medicines have been found acceptable, in principle, for procurement by UN agencies

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Background

A *Pilot Procurement, Quality, and Sourcing Project: Access to HIV/AIDS Drugs and Diagnostics of Acceptable Quality* was actively started in March 2001 by the World Health Organization (WHO) in collaboration with other United Nations (UN) agencies—UNAIDS, UNICEF, and UNFPA—with support from the World Bank.

The procedure for assessing the acceptability in principle of HIV/AIDS drugs comprises various components including:

1. The evaluation of product data and information provided by manufacturers and suppliers, and
2. Inspection of manufacturing sites.

Due to the particular properties of several substances used in some pharmaceutical finished dosage forms in the treatment of HIV/AIDS (eg, chiral activity, isomerism, sensitivity to relative humidity), and the current status where there are no pharmacopoeia monographs and standards available for several substances and finished products, WHO-appointed experts have performed a comprehensive and rigorous evaluation of the products included on the *Alphabetical Lists of Pre-Qualified Products Manufactured at Specified Manufacturing Sites*, with a view to [ascertaining] compliance with international standards (Table 1).

Objective

The objective of the project is to assess the acceptability in principle of HIV/AIDS

drugs for procurement by UN agencies. The assessment procedure is aimed at identifying products and suppliers meeting WHO standards. Thus, the project facilitates the procurement of HIV/AIDS-related drugs of acceptable quality.

Method followed for pre-qualification

In assessing HIV/AIDS-related drugs, the WHO *Guiding Principles for Evaluation of Manufacturers for the Procurement and Sourcing of Pharmaceutical Products*, has been followed.

The two main components of the assessment process are:

1. Dossier evaluation, and
2. Manufacturing site inspection.

Interested suppliers were requested to submit Expressions of Interest (EOI). The invitations for submitting EOI were published in October 2000 and August 2001. Product dossiers, containing product data and information for innovator and generic products, were requested for a thorough evaluation. The dossiers were evaluated in accordance with the requirements for the evaluation of multisource products.

Other criteria taken into account in the assessment process include:

- Valid regulatory approval to manufacture.
- Regulatory or other approval of the product in accordance with national requirements.
- Product manufactured in compliance with Good Manufacturing Practices (GMP) as

certified by the national regulatory authority and/or certified GMP inspectors.

- Product certificate exists in accordance with the WHO certification scheme on the quality of pharmaceutical products moving in international commerce.
- Product dossier of acceptable quality submitted and positive outcome of the assessment against the WHO recommended standards referred to below.
- Positive outcome of the inspection of the manufacturing site performed by inspectors appointed by the WHO.

In this voluntary assessment process, interested manufacturers were requested to submit product dossiers for various dosage forms and strengths of the products in the categories listed [below and] in Table 1.

Antiretroviral agents, including:

- Non-Nucleoside Reverse Transcriptase Inhibitors, such as Nevirapine, Efavirenz, and Delavirdine
- Nucleoside Reverse Transcriptase Inhibitors, such as Zidovudine, Didanosine, Zalcitabine, Stavudine, Lamivudine, Abacavir, and Lamivudine + Zidovudine
- Protease Inhibitors, such as Saquinavir, Ritonavir, Indinavir, Nelfinavir, Amprenavir, and Lopinavir + Ritonavir

Antibacterial and antimycobacterial agents, including: Azithromycin, Clarithromycin, Clindamycin, Ceftriaxone, Cefixime, Ciprofloxacin, and Rifabutin

Table1. Alphabetical List of Pre-Qualified Products Manufactured at Specified Manufacturing Sites

Ref. No.	International non-proprietary name (INN)	Strength	Dosage form	Supplier	Manufacturing site	Country	Packaging material and pack
106	Abacavir	300mg	Tablet	GlaxoSmithKline	GSK, Ware, Hertfordshire	UK	Blister 60
107	Abacavir	20mg/ml	Oral solution	GlaxoSmithKline	GSK, Speke, Liverpool	UK	HDPE (Bottle) 240ml
048	Aciclovir	5%	Cream	Cipla Ltd	Patalganga	India	Al tube G
112	Amprenavir	15mg/ml	Oral solution	GlaxoSmithKline	GSK, Speke, Liverpool	UK	HDPE (Bottle) 240ml
113	Amprenavir	50mg/150mg	Capsule	GlaxoSmithKline	RP Scherer, Beinhelm	France	HDPE (Bottle) 480 (50mg) 240 (150mg)
001	Ciprofloxacin	750mg	Tablet	Laboratorios Cinfa S.A.	Navara	Spain	Blister 10
002	Ciprofloxacin	500mg	Tablet	Laboratorios Cinfa S.A.	Navara	Spain	Blister 10/20
003	Ciprofloxacin	250mg	Tablet	Laboratorios Cinfa S.A.	Navara	Spain	Blister 10/20
056	Ciprofloxacin	100mg	Tablet	Cipla Ltd	Kurkumbh	India	Blister 10
057	Ciprofloxacin	250mg	Tablet	Cipla Ltd	Kurkumbh	India	Blister 10
058	Ciprofloxacin	500mg	Tablet	Cipla Ltd	Kurkumbh	India	Blister 10
059	Ciprofloxacin	750mg	Tablet	Cipla Ltd	Kurkumbh	India	Blister 10
065	Didanosine	25mg	Tablet	Bristol-Myers Squibb	Meymac	France	HDPE (Bottle) 60
066	Didanosine	50mg	Tablet	Bristol-Myers Squibb	Meymac	France	HDPE (Bottle) 60
067	Didanosine	100mg	Tablet	Bristol-Myers Squibb	Meymac	France	HDPE (Bottle) 60
068	Didanosine	150mg	Tablet	Bristol-Myers Squibb	Meymac	France	HDPE (Bottle) 60
069	Didanosine	200mg	Tablet	Bristol-Myers Squibb	Meymac	France	HDPE (Bottle) 60
053	Lamivudine	50mg/5	Solution	Cipla Ltd	Vikhroli	India	PET (Bottle) 100ml
117	Lamivudine	150mg	Tablet	GlaxoSmithKline	GSK, Ware, Hertfordshire	UK	HDPE (Bottle) 60
128	Lamivudine	10mg/ml	Oral Solution	GlaxoSmithKline	GSK, Speke, Liverpool	UK	HDPE (Bottle) 240ml
110	Lamivudine+ Zidovudine	150mg + 300mg	Tablet	GlaxoSmithKline	GSK, Ware, Hertfordshire	UK	Blister 60 HDPE (Bottle) 60
111	Lamivudine+ Zidovudine+ Abacavir	150mg+ 300mg+ 300mg	Tablet	GlaxoSmithKline	GSK, Ware, Hertfordshire	UK	Blister 40 HDPE (Bottle) 60 60
039	Nevirapine	200mg	Tablet	Cipla Ltd	Vikhroli	India	Blister 10
95	Ritonavir	100mg	Capsule	Abbott Laboratories	RP Scherer, Florida, or Beinhelm	USA France	HDPE (Bottle) 84
96	Ritonavir	80mg/ml	Oral solution	Abbott Laboratories	Queensborough, Kent	UK	PET (Bottle) 90ml
97	Ritonavir+ Lopinavir	33.3mg + 133.3	Capsule	Abbott Laboratories	RP Scherer, Florida	USA	Blisters 6 HDPE (Bottle) 90
98	Ritonavir+Lopinavir	20mg + 80mg/ml	Oral solution	Abbott Laboratories	Queensborough, Kent	UK	PET (Bottle) 60ml
133	Saquinavir	200 mg	Soft capsule	Roche	R.P. Scherer, Baden	Germany	6 + 180
061	Stavudine	15mg	Capsule	Bristol-Myers Squibb	Meymac	France	Blister 56 HDPE (Bottle) 60
062	Stavudine	20mg	Capsule	Bristol-Myers Squibb	Meymac	France	Al-PVC/PE/Aclar (Blister) 56
063	Stavudine	30mg	Capsule	Bristol-Myers Squibb	Meymac	France	Al-PVC/PE/Aclar (Blister) 56
064	Stavudine	40mg	Capsule	Bristol-Myers Squibb	Meymac	France	Al-PVC/PE/Aclar (Blister) 56
034	Sulfadiazine	500mg	Tablet	Doms Recordati	Saint Victor, Parc Mecatronic	France	Blister 10
050	Vinblastine sulfate	10mg/10ml	Injection	Cipla Ltd	Kurkumbh	India	Vial 10ml
042	Vincristine sulfate	1mg/ml	Injection	Cipla Ltd	Kurkumbh	India	Vial 1ml
141	Zalcitabine	0.375 mg	Tablet	Roche	Roche, New Jersey Basle	USA Switzerland	Blister (Al) 6 Glass bottle 100
142	Zalcitabine	0.75 mg	Tablet	Roche	Roche, New Jersey	USA	Blister (Al) 6 Glass bottle 100
027	Zidovudine	100mg	Capsule	Combino Pharm SL	Finaf 92, Gorgs y Lladó, Barabara del Valles or Medea, Santa Carolina, Barcelona	Spain	Al-Al STRIP 100
054	Zidovudine	50mg/5	Solution	Cipla Ltd	Vikhroli	India	PET (Bottle) 100ml
114	Zidovudine	10mg/ml	Infusion	GlaxoSmithKline	Catalytica Pharm. Inc, Greenville	USA	Amber Glass Vial 20ml
115	Zidovudine	50mg/5ml	Oral solution	GlaxoSmithKline	Wellcome Foundation, Dartford, Kent	UK	Amber glass bottle 200ml

Al: Aluminum; HDPE: High Density Polyethylene; PET: Polyethylene Terphthalate

Antiprotozoal agents, including: Trimethoprim/Sulphamethoxazole (IV), Pentamidine, Pyrimethamine, Sulfadiazine, and Folinic acid

Antiviral agents, including: Acyclovir, Cidofovir, Ganciclovir, and Foscarnet

Antifungal agents, including: Amphotericin B, Fluconazole, Itraconazole, and Ketoconazole

Anti-cancer drugs: Vinblastine, Etoposide, Bleomycin, and Vincristine

1. Dossier evaluation

Dossiers were thoroughly evaluated for compliance with WHO recommendations and guidelines regarding the assessment of multisource products (*Marketing Authorization of Pharmaceutical Products with Special Reference to Multisource (Generic) Products: A Manual for a Drug Regulatory Authority, WHO/DMP/RGS/98.5*) and bio-equivalence data (*Annex 9, WHO Technical Report Series No 863*), and ICH guidelines where appropriate to complement the aforesaid WHO recommendations and guidelines.

Each product dossier was evaluated by a team of evaluators (three for quality aspects, two for bio-availability/bio-equivalence). Suppliers were informed of the outcome of the evaluation and were given the opportunity to submit additional data and information requested.

To date [March 2002], 160 product dossiers for various products and dosage forms from 21 suppliers were received.

Some dossiers have now been fully evaluated and all the required data and information have been submitted. Those products that were found to comply with the standards referred to above, have been included in the list.

Several suppliers are currently still generating additional data and information on their products as part of the assessment process. In addition, new products may be submitted to the WHO for evaluation. If and when products will be found to meet the specified standards, they will be added to the list.

2. Inspections

In regard of products included in the list, inspections have been performed at the manufacturing sites (excluding those manufacturing sites that were recently inspected by regulatory authorities such as members from the Pharmaceutical Inspection Co-operation Scheme (PIC/S), or regulatory

authorities with equivalent quality systems). Manufacturers are inspected to assess compliance with GMP, as recommended by the WHO (*Quality Assurance of Pharmaceuticals. A Compendium of Guidelines and Related Materials. Volume 2. Good Manufacturing Practices and Inspection*). Several inspections have been performed, and others are due during 2002.

The inspections are performed by teams of inspectors. The teams consist of a WHO-appointed lead inspector (from countries that are members of the Pharmaceutical Inspection Co-operation Scheme, (PIC/S)), a WHO representative from the Department of Essential Drugs and Medicines Policy (EDM), Quality Assurance and Safety: Medicines (QSM) team in WHO, and an inspector(s) from the National Drug Regulatory Authority Inspectorate of the country in which the manufacturing site is located.

The inspection of the manufacturing site includes an in-depth evaluation to assess compliance with GMP. Specific focus is also placed on the manufacturing process of the products concerned (HIV/AIDS). Detailed inspection reports, listing all the observations and non-compliances have been drafted and were communicated to manufacturers after each inspection. Where deemed necessary, manufacturers have been required to implement corrective action to address deficiencies, before their product was included in the list.

Outcome of the pre-qualification

Only products and manufacturing sites found by the evaluators and inspectors to meet the recommendations as stipulated in the WHO guidelines referred to above are and will be included in the list of suppliers whose evaluated products are recommended by the WHO as being acceptable in principle for procurement by UN agencies (Table 1).

Future of the project

In view of the worldwide focus and importance of the treatment of HIV/AIDS, and to facilitate the access to HIV/AIDS drugs of acceptable quality, the project continues and additional product data and information will be evaluated, and manufacturing sites will be inspected. As these meet the specified standards, they will be added to the list.

The list will be reviewed and updated at regular intervals. Products and manufacturing sites included in the list will be re-assessed at regular intervals. Products

and manufacturing sites will be removed from the list, if as a result of a re-assessment, it is found that they no longer comply with the specified standards.

General notes

1. This list will be updated regularly. Other products are being and will be evaluated and will be added to the list as the data become available, the sites are inspected, and the product and manufacturing sites are found to meet the recommendations and standards as specified in the WHO documentation mentioned above.
2. This list indicates the products found to be acceptable in principle, as manufactured at the specified manufacturing sites.
3. The UN agency intending to use this list to procure products may wish to ensure that only products from the manufacturing sites mentioned in this list will be supplied by the supplier (same formula, manufacturing methods, manufacturing site as in the dossier provided for this project).
4. This list does not constitute any guarantee for the procurement of the products from the suppliers mentioned.
5. The fact that certain products and suppliers are not included in the list does not furthermore mean that if evaluated and tested, they could not be found to comply with the abovementioned standards.
6. This list may not be used by manufacturers and suppliers for commercial or promotional purposes.
7. This list is not an exhaustive list of pharmaceutical products used in the treatment of HIV/AIDS. It reflects those products for which data have been submitted and evaluated as a result of the Pilot Procurement, Quality, and Sourcing Project: Access to HIV/AIDS Drugs and Diagnostics of Acceptable Quality by interested suppliers which voluntarily participated in the assessment project. There is furthermore no guarantee that the products included in the list and found to comply with the abovementioned standards will continue to meet those standards.
8. This list reflects those products (manufactured at the specified manufacturing sites) with respect to which the product data and information submitted were found to meet the norms and standards recommended by the WHO. The manufacturing sites listed are those which

have subsequently, as part of the procedure, been found to meet the norms and standards recommended by the WHO at the time of inspection to assess compliance with GMP for the products listed. Inclusion in the list does not, however, imply any approval by the WHO of the products and manufacturing sites in question (which is the sole prerogative of national authorities).

9. It is recommended that prior to procurement, UN agencies familiarize themselves with aspects such as quantification and patents of the products in question as well as other related matters.
10. Assessment of additional products and manufacturing sites will be carried out at regular intervals.

Disclaimer

Inclusion in the list does not constitute an endorsement, or warranty of the fitness, of any product for a particular purpose, including in regard of its safety and/or efficacy in the treatment of HIV/AIDS. The WHO does not furthermore warrant or represent that: 1) the list is complete or error free; and/or that 2) the products and manufacturing sites which have been found to meet the standards recommended by the WHO, will continue to do so; and/or that 3) the products listed have obtained regulatory approval for use in the treatment of HIV/AIDS (or any other disease) in every country of the world, or that their use is otherwise in accordance with the national laws and regulations of any country, including but not limited to patent laws. In addition, the WHO wishes to alert procuring UN agencies that the improper storage, handling, and transportation of drugs may affect their quality, efficacy and safety. The WHO disclaims any and all liability and responsibility for any injury, death, loss, damage, or other prejudice of any kind whatsoever that may arise as a result of, or in connection with the procurement, distribution, and use of any product included in the list.

Acknowledgement

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US NIAID expands PACTG focus

The US National Institute of Allergy and Infectious Diseases (NIAID) recently announced US\$36 million in renewed funding for the Pediatric AIDS Clinical Trials Group (PACTG), and a greater focus on both adolescent research and international pediatric research. The new five-year awards will support 18 university-based clinical trials sites, a statistical and data management center, and a coordinating and operations center.

The PACTG has pioneered key trials evaluating treatments for children with HIV and has made great advances in reducing the rate of mother-to-infant HIV transmission in the developed world. The epidemic among adolescents in the United States, however, has become an increasing concern. The US Centers for Disease Control and Prevention reports that 4,219 cumulative cases of AIDS among adolescents, or children ages 13 through 19, were reported through June 2001,¹ and the number of adolescents living with HIV is estimated to be much higher. Because the average length of time between HIV infection and the development of AIDS is 10 years, it is believed that many adults became infected as adolescents. Most adolescents infected with HIV are at an early stage of disease and are ideal candidates for early intervention and treatment strategies.

HIV disease also continues to take a devastating toll on women and children in developing countries, where more than 90 percent of all HIV/AIDS cases occur. In 2001, approximately 2.7 million children younger than age 15 were living with HIV/AIDS worldwide, and 580,000 children in this age group died from HIV-associated illnesses or AIDS, according to a UNAIDS report.² In addition to the suffering of children, 48 percent of adults living with HIV/AIDS in the world are women, many of whom are of childbearing age.² To this end, the PACTG will also directly support clinical research at four international sites, two in South Africa and two in Thailand.

"The Pediatric AIDS Clinical Trials Group has been instrumental in forging new prevention and treatment strategies for HIV-

infected mothers and their children, and in working to extend and improve the quality of their lives," said NIAID Director Anthony S. Fauci. "As the global scope of the epidemic evolves, the PACTG will continue to tackle the most critical needs in pediatric and adolescent HIV/AIDS research both in the United States and the developing world."

The PACTG's new research agenda emphasizes five key areas:

Perinatal Transmission: Continue studying the safety of antiretroviral drugs in HIV-infected pregnant women; continue translational research for resource-poor international partners; and examine why current interventions are not fully successful.

Pediatric Treatment: Study the safety of new drugs, the best use of available drugs and treatment management; and evaluate the effect of interventions on the course of the disease.


Adolescent Treatment: Expand adolescent research to every PACTG site; study the effects of treatment on acute and early infection and on restoration of immune function; and promote collaborations to assist in prevention research, including behavioral research.

Long-term Evaluation of Antiretroviral Therapies: Increase commitment to long-term pediatric studies; study drug safety in infants who escape infection and in children who become infected; and link durability of treatment responses to clinical outcomes.

Domestic and International Collaborations: Collaborate with other US National Institutes of Health (NIH)-sponsored domestic and international HIV/AIDS therapeutic and prevention trials networks; encourage scientific exchange and resource-sharing with international partners; and conduct international studies of interventions that can be readily transferred to developing countries. ■

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- 2 UNAIDS. Report on the Global HIV/AIDS Epidemic: December 2001.



Scaling Up Antiretroviral Therapy in Resource- Limited Settings: *Guidelines for a Public Health Approach*

*Executive Summary
April 2002*

This is the Executive Summary of “Scaling Up Antiretroviral Therapy in Resource-Limited Settings: Guidelines for a Public Health Approach,” edited by Scott Hammer, Columbia University, New York City, USA, Editor-in-Chief; Diana Gibb, British Medical Research Council, London, UK, Editor, Pediatric Chapter; Diane Havlir, University of California at San Diego, USA, Editor, HIV-Related Co-Infections Chapter; Lynne Mofenson, National Institutes of Health, NICHD, Bethesda, USA, Editor, Pregnancy Chapter; Ingrid Van Beek, Sydney Hospital, Sydney, Australia, Editor, Injection Drug User’s Chapter; Stefano Vella, Istituto Superiore de Sanita, Rome, Italy, Editor, Clinical and Laboratory Monitoring of ARV Use Chapter. Coordinated by: Basil Vareldzis and Jos Perriens of the HIV/AIDS Department of the World Health Organization (WHO), Geneva.

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Introduction

Less than a decade ago, when the one available class of antiretroviral (ARV) drugs was unable to adequately inhibit replication of the human immunodeficiency virus (HIV), the lives of people living with HIV/AIDS the world over followed an often immutable course: gradual destruction of the immune system, initiation of prophylaxis to prevent opportunistic infections, early retirement, wasting, periods of wellness and illness punctuating an inexorable decline towards complete immune depletion and finally, death.

Since 1996, the advent of new classes of ARV drugs and their use in combination have changed the way people in the world’s richest countries think about HIV/AIDS. Although these treatments are not a cure and present new challenges of their own to people living with HIV/AIDS, they have dramatically improved rates of mortality and morbidity, prolonged lives, improved quality of life, revitalized communities and transformed perceptions of HIV/AIDS from a plague to a manageable, chronic illness.

Unfortunately, most of the 36 million people in the developing world currently living with HIV/AIDS do not share this vastly improved prognosis. WHO conservatively estimates that in 2002, some 6 million people in resource-limited settings

are in need of life-sustaining ARV therapy now. Instead, only 230,000 have access to them, and half of these live in one country, Brazil.

In the wake of the [XIII] International AIDS Conference in Durban [, South Africa,] in 2000, and the United Nations General Assembly Special Session on HIV/AIDS (UNGASS) in 2001, the resolve of the international community to address this appalling disparity between treated and untreated, between rich and poor, is stronger than ever before. The world recognizes the pressing moral, social, political and economic imperatives to expand access to antiretroviral therapy to many more millions of people living with HIV/AIDS as soon as practicable, and has begun to mobilize the “great global alliance” which UN Secretary-General Kofi Annan has called for to achieve the UNGASS goals.

These guidelines are part of the World Health Organization’s ongoing commitment to this great global alliance. Their development involved a year long process of international consultative meetings in 2001, in which more than 200 clinicians, scientists, government representatives, representatives of civil society, and people living with HIV/AIDS from more than 60 countries participated. The recommenda-

tions included in this document reflect the best current practices based on a review of existing evidence. Where the body of evidence was not conclusive, expert consensus was used as a basis for recommendations. In this rapidly evolving field, the WHO recognizes that these recommendations will need to be updated on a regular basis.

Although it is an important step, this document is not intended to be a “magic bullet” for expanding access to ARV treatment. Drug access for the millions who need it will be improved not only by guidance on the rational selection and use of ARV drugs, but also by improved affordability and sustainability of drug financing and by accessible, appropriate and competent health services. These other critical elements continue to be promoted by actors within and beyond the UN system in the following ways:

- The Accelerating Access Initiative, which has led to dramatic reductions in the cost of ARV drugs in 20 developing countries by January 2002;
- The mapping of sources and prices of HIV-related drugs by UNICEF, UNAIDS, Médecins-Sans-Frontières (MSF), and the WHO;
- The assessment of the patent situation for HIV-related drugs by the WHO and UNAIDS;
- Increased financial and human resources for efforts by the WHO to strengthen health systems capacity in HIV/AIDS, including the launch of an international network of training institutions for HIV care; [and]
- The Global Fund to Fight AIDS, Tuberculosis and Malaria, launched by UN Secretary-General Kofi Annan in 2001, involving a significant new investment of financial resources against these three major infectious diseases.

Document objectives

Currently, fewer than five percent of those who require ARV treatment can access these medicines in resource-limited settings. The WHO believes that at least three million people needing care should be able to get medicines by 2005—a more than ten-fold increase.

These guidelines are intended to support and facilitate the proper management and scale-up of ART in the years to come by proposing a public health approach to achieve these goals. The key tenets of this approach are:

- 1) Scaling up of antiretroviral treatment programs to meet the needs of people living with HIV/AIDS in resource-limited settings;
- 2) Standardization and simplification of ARV regimens to support the efficient implementation of treatment programs; [and]
- 3) Ensuring that ARV treatment programs are based on the best scientific evidence, in order to avoid the use of substandard treatment protocols which compromise the treatment outcome of individual clients and create the potential for emergence of drug resistant virus.

While it is hoped that this document will be useful to clinicians in resource-limited settings, it is intended primarily for use by Treatment Advisory Boards, national AIDS program managers, and other senior level policymakers involved in the planning of national and international HIV care strategies in resource-limited settings. The guidelines serve as a framework for selecting the most potent and feasible antiretroviral regimens as part of an expanded national response. The framework aims to “standardize” and simplify antiretroviral therapy, much like tuberculosis (TB) treatment in national TB control programs, while acknowledging the relative complexity of HIV treatment. Accordingly, options for first- and second-line regimens are presented, bearing in mind the needs of health systems that often lack sophisticated manpower and monitoring facilities, without compromising the quality and outcomes of the treatments offered.

The topics addressed in these guidelines include [antiretroviral therapy (ART)], which ARV regimens to start, reasons for changing ART, and what regimens to continue if treatment needs to be changed. It also addresses how treatment should be monitored, with specific reference to the side effects of ART, and makes specific recommendations for certain patient subgroups.

When to start ARV therapy

The WHO recommends that in ARV treatment programs in resource-limited settings HIV-infected adolescents and adults should start ARV therapy when they have:

- WHO stage IV of HIV disease (clinical AIDS), regardless of CD4 count
- WHO Stages I, II or III of HIV disease, with a CD4 count below 200/mm³
- WHO Stages II or III of HIV disease with TLC below 1200/mm³

Wherever possible, countries are encouraged to use CD4 cell counts in their ARV treatment programs and consider the use of simple, low cost CD4 methodologies that are currently available to enable the wider use of CD4 cell counts in their programs. However, in cases where CD4 counts cannot be assessed, the presence of a total lymphocyte count below 1200/mm³ may be used as a substitute indication for treatment in the presence of symptomatic HIV disease (ie, WHO stages II or III). While the total lymphocyte count correlates relatively poorly with CD4 count, in combination with clinical staging it is a useful marker of prognosis and survival. An assessment of viral load (eg, using plasma HIV-1 RNA levels) is not considered essential to start therapy.

In children, the WHO recommends offering ARV combination therapy to HIV-positive infants under the age of 18 months if they have virologically proven infection (using either HIV PCR or immune complex dissociated HIV p24 antigen detection or HIV culture) and WHO Pediatric Stage III HIV disease (ie, clinical AIDS) or WHO Pediatric Stages I and II disease and a CD4 percentage <20%. In settings where virologic confirmation is not available, ARV combination therapy can be offered to HIV-positive infants who have WHO Stage III HIV disease and have a CD4 percentage <20%. For children over the age of 18 months who are HIV antibody positive, the WHO recommends ART if they have WHO Stage III HIV disease (ie, clinical AIDS) regardless of CD4 percentage. For those older children with WHO stage I or II HIV disease, ART is recommended if the CD4 percentage is <15%.

Recommended first-line regimens in adults

Countries are encouraged to use a public health approach to facilitate the scale-up of ARV use in resource-limited settings. This means that antiretroviral treatment programs should be developed and requires that ARV treatment be standardized. In particular, it is suggested that countries select a single first and a limited number of second line regimens for large scale use, recognizing that individuals who cannot tolerate or fail the first and second line regimens would be referred for individualized care by specialist physicians.

Table 1. Recommendations for initiating anti-retroviral therapy in adults and adolescents with documented HIV infection

If CD4 testing available:

- WHO Stage IV disease irrespective of CD4 cell count
- WHO Stage I, II or III* with CD4 cell counts below 200/mm³†

If CD4 testing unavailable:

- WHO Stage IV disease irrespective of total lymphocyte count
- WHO Stage II or III* disease with a total lymphocyte count below 1200/mm³‡

* Treatment is also recommended for patients with advanced WHO Stage III disease including recurrent or persistent oral thrush and recurrent invasive bacterial infections irrespective of CD4 cell or total lymphocyte count.

† The precise CD4 level above 200/mm³ at which to start ARV treatment has not been established but the presence of symptoms and the rate of CD4 cell decline (if measurement available) should be factored into the decision making. A CD4 level of 200/mm³ corresponds to a CD4 percentage of approximately 15%.

‡ A total lymphocyte count of below 1200/mm³ can be substituted for the CD4 count when the latter is unavailable and HIV-related symptoms exist. It is less useful in the asymptomatic patient. Thus, in the absence of CD4 cell testing, asymptomatic HIV infected patients (WHO Stage I) should not be treated because there is currently no other reliable marker available in severely resource constrained settings.

Considerations in the selection of ARV treatment regimens at both the program level and at the level of an individual patient should include the potency, side effect profile, the potential for maintenance of future treatment options, the anticipated adherence of the patient population with a regimen, coexistent conditions (eg, co-infections, metabolic abnormalities), pregnancy or the risk thereof, the use of concomitant medications (ie, potential drug interactions), the potential for primary acquisition of resistant viral strains, and cost and access. Additional considerations relevant to resource-limited settings may include access to only a limited number of ARV drugs, limited health service infrastructure, the need to deliver drugs to rural areas, a high incidence of tuberculosis and hepatitis B and/or C, and the presence of varied HIV groups and subtypes.

Taking all of these considerations except the cost of drugs into account, the preferred first-line antiretroviral regimens in adults and adolescents are listed in the Table 3. All regimens consist of a dual nucleoside

Table 2. Recommendations for initiating antiretroviral therapy in infants and children

CD4 testing	Age	HIV diagnostic testing	Treatment recommendation
If CD4 testing is available	< 18 months	Positive HIV virologic test*	<ul style="list-style-type: none"> • WHO Pediatric Stage III (AIDS), irrespective of CD4 cell percentage† • WHO Pediatric Stage I disease (asymptomatic) or Stage II disease with CD4 percentage < 20%‡
		HIV virologic testing not available but infant HIV seropositive or born to known HIV-infected mother (Note: HIV antibody test <i>must</i> be repeated at age 18 months to obtain definitive diagnosis of HIV infection)	<ul style="list-style-type: none"> • WHO Pediatric Stage III disease (AIDS) with CD4 cell percentage < 20%
If CD4 testing is not available	≥18 months	HIV antibody seropositive	<ul style="list-style-type: none"> • WHO Pediatric Stage III disease (AIDS) irrespective of CD4 cell percentage† • WHO Pediatric Stage I disease (asymptomatic) or Stage II disease with CD4 percentage < 15%‡
		Positive HIV virologic test	<ul style="list-style-type: none"> • WHO Pediatric Stage III†
If CD4 testing is not available	< 18 months	HIV virologic testing not available but infant HIV seropositive or born to known HIV-infected mother.	<ul style="list-style-type: none"> • Treatment not recommended**
		HIV antibody seropositive	<ul style="list-style-type: none"> • WHO Pediatric Stage III†

* HIV DNA PCR or HIV PCR RNA or immune complex dissociated p24 antigen assays, or HIV culture.

† Initiation of ARV can also be considered for children who have advanced WHO Pediatric Stage II disease including such as severe recurrent or persistent oral candidiasis outside the neonatal period, weight loss, fevers, or recurrent severe bacterial infections, irrespective of CD4 count.

‡ The rate of decline in CD4 percentage (if measurement available) should be factored into the decision making.

** Many of the clinical symptoms in the WHO Pediatric Stage II and III disease classification are not specific for HIV infection and significantly overlap with those seen in children without HIV infection in resource-limited settings; thus, in the absence of virologic testing and CD4 cell assay availability, HIV-exposed infants ≤18 months of age should generally not be considered for ART regardless of symptoms.

component, and a potent third drug to complement it. Zidovudine (ZDV)/lamivudine (3TC) is listed as the initial recommendation for the dual nucleoside component based on efficacy, toxicity, clinical experience and the availability of ZDV/3TC as a fixed dose combination. Other dual nucleoside combinations can be substituted for ZDV/3TC, including stavudine (d4T)/3TC, d4T/didanosine (ddI) and ZDV/ddI depending upon country-specific preferences. However, ZDV/d4T should never be used together because of proven antagonism between the two drugs.

Of note is that dual nucleoside drug regimens alone are no longer recommended as they do not adequately suppress HIV replication and are likely to lead to the rapid emergence of resistance.

In the dual nucleoside plus non-nucleoside regimens, the advantage is that the drugs are widely available at affordable cost

and reasonable pill counts, and the regimens are potent. The main disadvantages are development of drug resistance, the potential hepatotoxicity of nevirapine (NVP), and the need to have separate regimens for men and women due to the potential teratogenic effects of efavirenz (EFZ), which precludes its use in pregnant women or women of childbearing age who are at risk of an unintended pregnancy. Countries with a significant prevalence of HIV-2 as well as Group O HIV-1 viruses might consider reserving the use of the non-nucleoside-containing regimens to patients with proven HIV-1 infection, as HIV-2 as well as Group O HIV-1 viruses are naturally resistant to this class of drugs.

The ZDV/3TC/abacavir (ABC) regimen is the most user-friendly from both a patient and program perspective (2 pills a day and absence of significant drug interactions). Its main disadvantages are some uncertainty

Table 3. Recommended first-line ARV combination regimens in adults and adolescents with documented HIV infection

Regimen*	Pregnancy considerations	Major toxicities
ZDV/3TC/EFZ or ZDV/3TC/NVP	<ul style="list-style-type: none"> Substitute NVP for EFZ in pregnant women or women for whom effective contraception cannot be assured 	<ul style="list-style-type: none"> ZDV-related anemia EFZ-associated CNS symptoms Possible teratogenicity of EFZ NVP-associated hepatotoxicity and severe rash
ZDV/3TC/ABC	<ul style="list-style-type: none"> ABC safety data limited 	<ul style="list-style-type: none"> ZDV-related anemia ABC hypersensitivity
ZDV/3TC/RTV-PI† or ZDV/3TC/NFV	<ul style="list-style-type: none"> LPV/r safety data limited NFV: most supportive safety data 	<ul style="list-style-type: none"> ZDV-related anemia NFV-associated diarrhea IDV-related nephrolithiasis PI-related metabolic side effects

*ZDV/3TC is listed as the initial recommendation for dual NsRTI component based on efficacy, toxicity, clinical experience and availability of fixed dose formulation. Other dual NsRTI components can be substituted including d4T/3TC, d4T/ddI and ZDV/ddI depending upon country-specific preferences. ZDV/d4T should never be used together because of proven antagonism.

† RTV-PI includes IDV/r, LPV/r, and SQV/r.

Table 4. Recommended second-line regimens in adults and adolescents

First-line regimens	Second-line regimens for treatment failure	Alternative second-line regimen for treatment failure
ZDV/3TC/EFZ or ZDV/3TC/NVP	RTV-PI* + d4T/ddI	RTV-PI + ABC/ddI, NFV + ABC/ddI or NFV + d4T/ddI
ZDV/3TC/ABC	NNRTI† + LPV/r with or without d4T or ddI	RTV-PI + d4T/ddI
ZDV/3TC/RTV-PI or ZDV/3TC/NFV	NNRTI† + d4T/ddI	NNRTI† + ABC/ddI

* RTV-PI can be either IDV/r, LPV/r or SQV/r

† NNRTI can be either EFV or NVP

whether it works when viral load is very high in patients with very advanced disease, uncertainty that the drugs—in particular ABC—will become available at an affordable cost, and the potential of causing fatal hypersensitivity reactions that could escape detection in resource-poor settings. There is relatively limited data on the efficacy of other potential triple nucleoside reverse transcriptase inhibitor (NsRTI) combinations. This precludes the WHO from recommending them at this time.

Advantages of the dual nucleoside plus protease inhibitor (PI) regimen are proven high potency in reducing viral loads. Disadvantages are higher pill counts, significant interactions with other drugs that preclude or complicate their use during TB treatment using rifampicin, metabolic abnormalities and the need for a functioning cold chain for ritonavir-boosted regimens.

Reasons for changing ARV therapy

ART may need to be changed for either treatment failure or toxicity. Treatment failure can be evaluated clinically, immunologically using measurement of the CD4 count, and/or virologically by measuring viral loads. However, as the latter are not normally available in resource-limited settings, it is recommended that programs in such settings should primarily use clinical and where possible CD4 count criteria to define treatment failure.

Toxicity is related to the inability to tolerate the side effects of the medication and to significant organ dysfunction that may result. This can be monitored clinically based on patient reports and physical examination, and may include a limited number of laboratory tests depending on the specific combination regimen that is utilized.

If a change in regimen is needed because of treatment failure a new second line regimen will need to be used. If it is indicated because of toxicity, either an entirely new second line regimen can be prescribed, or, when the toxicity is related to an identifiable drug in the regimen, the offending drug can be replaced with another drug that does not have the same side effects.

Choice of second-line ARV regimens

The WHO recommends that the full regimen be changed from a first to a second line combination regimen in the case of treatment failure. The new second line regimen will need to use drugs which retain activity against the patient's virus strain and ideally include at least three new drugs, with at least one from a new class, in order to increase the likelihood of treatment success and minimize the risk of cross resistance.

Table 4 lists the second line regimens one could consider in adolescents and adults for each of the first line regimens identified in Table 1. A reasonable dual nucleoside component alternative to ZDV/3TC is d4T/ddI. In addition, ZDV/ddI can replace d4T/3TC and vice versa with the caveat that nucleoside analog cross resistance is an increasing concern.

When ZDV/3TC was used in the first line regimen, nucleoside cross-resistance may compromise the potency of d4T/ddI in the second line regimen, in particular in the presence of long-standing virologic treatment failure. As the chances of cross-resistance are somewhat reduced when switching to ABC/ddI compared to switching to d4T/ddI, the former might also be considered as the nucleoside backbone for a second line regimen if the first line regimen did not include ABC. However, high level ZDV/3TC resistance also confers diminished susceptibility to ABC.

Given the diminished potential of almost any second line nucleoside component, an RTV-PI component [indinavir (IDV)/r, lopinavir (LPV)/r, saquinavir (SQV)/r] is preferred to nelfinavir (NFV) in second line regimens given their potency. NFV can be considered as an alternative for the PI component if an RTV enhanced PI is not available or if there is a clinical contraindication to its use.

Table 5. Recommended first-line antiretroviral regimens for children*

Regimen	Comments
ZDV/3TC+ plus ABC	Preferred if concomitant anti-tuberculosis therapy being received
ZDV/3TC+ plus NNRTI	NNRTI choice: <ul style="list-style-type: none"> • if < 3 years or < 10 kg, NVP • if ≥ 3 years or ≥ 10 kg, NVP or EFV

* Country-specific considerations and preferences should determine which regimen or regimens to make available.

† ZDV/3TC is the first choice dual NRTI regimen for children as it has the largest amount of clinical experience. Other dual NRTI components can be substituted for children, including ZDV/ddI, d4T/3TC, d4T/ddI, and ddI/3TC. ZDV/d4T should never be used together due to proven antagonism.

Table 6. Recommended second-line antiretroviral regimens for children

First-line regimen	Second-line regimens
ZDV/3TC/ABC	d4T/ddI/LPV/r* or d4T/ddI/NFV or d4T/ddI/NNRTI†
ZDV/3TC/NNRTI†	d4T/ddI/LPV/r* or d4T/ddI/NFV

* For children who can swallow capsules and for whom the current capsule formulations allow appropriate weight or body surface area calculated dosing, additional options to replace LPV/r include SQV/r and IDV/r.

† NNRTI choice: if < 3 years or < 10 kg, NVP; if ≥ 3 years or ≥ 10 kg, NVP or EFV.

Considerations for specific subgroups of patients

Women of childbearing potential or who are pregnant

The WHO recommends the use of ZDV, 3TC, NVP, NFV and SQV combined with low dose ritonavir, as these have been the most widely used ARVs in pregnant women. EFZ is not recommended for use in women who could become pregnant due to its potential teratogenic effect on the fetus in the first trimester.

The choice of ART in women with the potential to become pregnant must include consideration of the possibility that the ARV drugs may be received during the early first trimester, prior to recognition of pregnancy and during the primary period of fetal organ development. Women who are receiving ART should have available to them effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy. It is important to note that some antiretroviral drugs (the NNRTIs NVP and EFZ and all the RTV boosted PIs) can lower blood concentrations of oral contraceptives and additional or alternative contraception needs to be used to avoid pregnancy in women receiving these drugs.

For pregnant women, it may be desirable

to initiate ART after the first trimester, although for pregnant women who are severely ill, the benefit of early therapy outweighs any potential fetal risks. Additionally, the dual NRTI combination of d4T/ddI should only be used during pregnancy when no other alternatives exist, due to the potential increased risk of lactic acidosis with this combination in pregnant women.

Children

The limited studies of HAART in children suggest that broadly similar improvements are seen in surrogate markers with many different ART regimens.

Most ARVs available for adults are also available for children with specific child formulations including dosages that are based on either body surface area or weight. First line treatment options for children include ZDV/3TC plus either a non-nucleoside (NVP or EFZ) or ABC. A caveat is that EFZ cannot be used in children under the age of three years due to lack of appropriate dosing information. However, EFZ would be the non-nucleoside of choice in children on rifampicin, in case ARV needs to start before anti-tuberculous therapy is completed. Second line therapy for children in the event of first-line regimen failure

would include a change in nucleoside backbone (eg, from ZDV+3TC to d4T+ddI) plus a protease inhibitor. Use of protease inhibitors other than LPV/r and NFV is problematic in children due to lack of suitable pediatric drug formulations for IDV and SQV.

People with tuberculosis and HIV co-infection

The WHO recommends that people with TB/HIV complete their TB therapy prior to beginning ARV treatment unless there is a high risk of HIV disease progression and death during the period of TB treatment (ie, a CD4 count <200/mm³ or disseminated TB is present). In cases where a person needs TB and HIV treatment concurrently, first line treatment options include ZDV/3TC or d4T/3TC plus either a non-nucleoside or ABC. If a non-nucleoside regimen is used, EFZ would be the preferred drug as its potential to aggravate the hepatotoxicity of TB treatment appears less than that of NVP. However, its dosage may need to be increased to 800 mg/day. Except for SQV/r, protease inhibitors are not recommended during TB treatment with rifampicin due to their interactions with the latter drug.

Injecting drug users

Injecting drug users who are eligible for ART should be ensured access to this life saving therapy. Special considerations for this population include dealing prospectively with life style instability which challenges drug adherence and accounting for the potential drug interactions of ARVs with agents such as methadone. Development of programs which integrate care of drug dependence and HIV is encouraged. In such settings, approaches such as directly observed therapy can be implemented. Once daily ARV regimens are already being explored in this arena and lend themselves to such approaches.

Adherence to antiretroviral therapy

The WHO recommends that innovative approaches to enhance adherence to ART be developed, due to the lifelong nature of this treatment.

Strategies to enhance adherence include minimizing pill counts and dosage frequencies by preferentially using combination pills on a once or twice daily basis.

Table 7. Antiretroviral therapy for individuals with tuberculosis co-infection

<i>Situation</i>	<i>Recommendations</i>
Pulmonary TB and CD4 count <50/mm ³ or extrapulmonary TB	Start TB therapy. Start one of these ARTs as soon as TB therapy is tolerated: ZDV/3TC/ABC ZDV/3TC/EFZ ZDV/3TC/SQV/r ZDV/3TC/NVP
Pulmonary TB and CD4 50 - 200/mm ³ or total lymphocyte count below 1200/mm ³	Start TB therapy. Start one of these regimens after completing 2 months of TB therapy: ZDV/3TC/ABC ZDV/3TC/EFZ ZDV/3TC/SQV/r ZDV/3TC/NVP
Pulmonary TB and CD4 >200/mm ³ or total lymphocyte count ≥1200/mm ³	Treat TB. Monitor CD4 counts if available. Start ART according to Tables 1 or 2 after completion of TB treatment.

A number of fixed dose combination products containing two or three ARV drugs are currently marketed that can be used twice a day. However, while a number of ARV drugs have now been approved for once daily administration, relatively few three or four drug once daily regimens have been rigorously tested in clinical trials. Other approaches which might facilitate adherence include: enlisting the assistance of family or community members to support patients in taking their medications on a regular and timely basis; extensive counseling and patient education; and directly observed therapy. Psychosocial issues that can also contribute to low adherence to therapy need to be taken into consideration especially for injection drug users and other vulnerable populations.

Drug resistance surveillance

The WHO recommends that countries planning to implement ART programs also concurrently implement an HIV drug resistance sentinel surveillance system. This will allow countries to detect potential drug resistance at the population level and modify recommended treatment regimens accordingly. A Global HIV Drug Resistance Surveillance Network is being established by the WHO in collaboration with partner organizations to assist member states in this area.

Clinical and laboratory monitoring of antiretroviral use

The WHO recommends that in resource-limited settings the basic clinical assessment

prior to the initiation of ART include documentation of past medical history, identification of current and past HIV-related illnesses, identification of co-existing medical conditions that may influence choice of therapy (such as TB or pregnancy) as well as current symptoms and physical signs.

In order to facilitate the scale up [of] ARV use in resource-limited settings, the WHO prioritized currently available testing into four categories:

- absolute minimum tests;
- basic recommended tests;
- desirable tests; and
- optional tests.

Absolute minimum tests are prerequisites for introduction of ARV therapy in a national program. Basic recommended tests are commonly used in the clinical setting and are needed to provide effective monitoring of most ARV regimens. In light of the urgency to provide potentially life prolonging care to so many millions of people, the WHO wants to minimize the impediments to care. As such, the basic recommended lab tests were not considered to be absolutely essential to start treatment, although they need to be available where resources are available. Desirable tests would make monitoring and evaluation of program effectiveness much more effective, while optional tests can be used in resource-rich settings.

The absolute minimum laboratory tests to have before initiating ART are an HIV antibody test and a hemoglobin or hemat-

ocrit level. The rationale is that proof of HIV infection is needed prior to starting ARV therapy in the first instance, and screening for anemia is essential prior to starting zidovudine containing regimens.

Basic recommended testing should include a white blood cell count and differential (to permit assessment of neutropenic side effects and the total lymphocyte count), serum alanine or aspartate aminotransferase level to assess the possibility of hepatitis co-infection and to monitor for hepatotoxicity, serum creatinine and/or blood urea nitrogen to assess baseline renal function, a serum glucose, and pregnancy tests for women. While these tests are not absolutely essential, they are highly recommended in order to be able to provide monitoring for safe use of these agents and inform decisions about switching between regimens. CD4 cell counts are at present not listed as basic recommended tests. However, it is hoped that with introduction of simple and less costly methods to assess CD4 cell counts, these tests will become more widely available. The WHO recommends that this be considered a priority issue because CD4 cell counts are the best indicator of immunologic response to treatment.

Desirable tests include bilirubin, amylase and serum lipids and CD4 cell testing. These tests, while not absolutely essential, are felt to provide significant information that would be beneficial in the monitoring of ARV use in resource-limited settings.

Viral load testing is currently considered optional because of resource constraints. Clinical monitoring is essential for the provision of safe and effective ARV therapy. Where laboratory monitoring is limited, close clinical monitoring becomes even more crucial.

The WHO also has categorized laboratory tests according to the levels in the health service where they could be used. Simple rapid HIV diagnostic tests and sample referral for CD4 testing should be feasible at the primary healthcare and district level. District level facilities should also be able to offer pregnancy testing, hemoglobin, liver function tests, creatinine, and glucose testing. In addition to the above mentioned tests, provincial level facilities should be able to offer CD4 cell tests.

Viral load testing and viral resistance assays would, resources permitting, be made available at the central level. ■

Appendices

Appendix A. Dosages of antiretroviral drugs for adults and adolescents*

Drug class	Drug	Dose
Nucleoside RTIs	Zidovudine (ZDV)	300 mg twice daily
	Stavudine (d4T)	40 mg twice daily (30 mg twice daily if < 60 kg)
	Lamivudine (3TC)	150 mg twice daily
	Didanosine (ddl)	400 mg once daily (250 mg once daily if < 60 kg)
	Abacavir (ABC)	300 mg twice daily
Nucleotide RTI	Tenofovir (TDF)	300 mg once daily
Non-Nucleoside RTIs	Efavirenz (EFZ)	600 mg once daily
	Nevirapine (NVP)	200 mg once daily for 14 days, then 200 mg twice daily
Protease inhibitors	Nelfinavir (NFV)	1,250 mg twice daily
	Indinavir/ritonavir (IDV/r)	800 mg/100 mg twice daily ^{†, **}
	Lopinavir/ritonavir (LPV/r)	400 mg/100 mg twice daily (533 mg/133 mg twice daily when combined with EFZ or NVP)
	Saquinavir/ritonavir (SQV/r)	1,000 mg/100 mg twice daily ^{‡, **}

* These dosages are in common clinical use. The dosages featured in this table were selected based on the best available clinical evidence. Dosages that can be given on a once or twice daily basis were preferred in order to enhance adherence to therapy. The doses listed are those for individuals with normal renal and hepatic function. Product specific information should be consulted for dose adjustments that may be indicated with renal or hepatic dysfunction or for potential drug interactions with other HIV and non-HIV medications.

† This dosage regimen is in common clinical use. Other IDV/r dosage regimens that range from 800 mg/200 mg bid to 400 mg/100 mg bid are also in clinical usage.

‡ Both the hard-gel and soft-gel capsule formulations can be used when SQV is combined with RTV.

** Dosage adjustment when combined with an NNRTI is indicated but a formal recommendation cannot be made at this time. One consideration is to increase the RTV component to 200 mg bid when EFZ or NVP is used concomitantly. More drug interaction data are needed.

Appendix B. Summary of pediatric drug formulations and doses

Name of drug	Formulations	Pharmacokinetic data available	Age (WEIGHT), DOSE* and DOSE frequency	Other comments
Nucleoside ANALOGUE reverse transcriptase inhibitors				
Zidovudine (ZDV)	Syrup: 10 mg/ml Capsules: 100 mg; 250 mg Tablet: 300 mg	All ages	< 4 weeks: 4 mg/kg/dose twice daily 4 weeks to 13 yrs: 180 mg/m ² /dose twice daily Maximum dose: ≥13 yrs: 300 mg/dose twice daily	Large volume of syrup not well tolerated in older children. Needs storage in glass jars and is light sensitive. Can give with food. Doses of 600 mg/m ² /dose twice daily required for HIV encephalopathy. Do not use with d4T (antagonistic antiretroviral effect).
Lamivudine (3TC)	Oral solution: 10 mg/ml Tablet: 150 mg	All ages	< 30 days: 2 mg/kg/dose twice daily ≥30 days or < 60 kg: 4 mg/kg/dose twice daily Maximum dose: > 60 kg: 150 mg/dose twice daily	Well tolerated. Can give with food. Store solution at room temperature (use within one month of opening).
Fixed-dose combination of ZDV plus 3TC	No liquid available Tablet: 300 mg ZDV plus 150 mg 3TC	Adolescents and adults	Maximum dose: > 13 yrs or > 60 kg: 1 tablet/dose twice daily	Tablet should not be split.
Didanosine (ddl, dideoxyinosine)	Oral suspension pediatric powder/water: 10 mg/ml. In many countries needs to be made up with additional antacid. Chewable tablets: 25 mg; 50 mg; 100 mg; 150 mg; 200 mg. Enteric-coated beadlets in capsules: 125 mg; 200 mg; 250 mg; 400 mg	All ages	< 3 mos: 50mg/m ² /dose twice daily. 3 mos to < 13 yrs: 90 mg/m ² /dose twice daily or 240 mg/m ² /dose once daily Maximum dose: ≥13 yrs or > 60 kg: 200 mg/dose twice daily or 400 mg once daily	Keeps suspension refrigerated; stable for 30 days; must shake well. Ideally taken 1 hour or 2 hours after food; may be less important in children. Enteric-coated beadlets in capsules can be opened and sprinkled on small amount of food.

* Meter² body surface area calculation: square root of (height in centimeters times weight in kilograms divided by 3600).

Appendix B. Summary of pediatric drug formulations and doses* (Cont'd)

Name of drug	Formulations	Pharmacokinetic data available	Age (WEIGHT), DOSE* and DOSE frequency	Other comments
Nucleoside ANALOGUE reverse transcriptase inhibitors (cont'd)				
Stavudine (d4T)	Oral solution: 1 mg/ml Capsules: 15 mg, 20 mg, 30 mg, 40 mg	All ages	< 30kg: 1 mg/kg/dose twice daily 30 to 60 kg: 30 mg/dose twice daily Maximum dose: > 60 kg: 40 mg/dose twice daily	Large volume of solution. Keep solution refrigerated; stable for 30 days; must shake well. Needs to be stored in glass bottles. Capsules opened up and mixed with small amount of food are well tolerated (stable in solution for 24 hours if kept refrigerated). Do not use with AZT (antagonistic antiretroviral effect).
Abacavir (ABC)	Oral solution: 20 mg/ml Tablet: 300 mg	Over age 3 months	< 16 years or ≤37.5 kg: 8 mg/kg/dose twice daily Maximum dose: >16 years or >37.5 kg: 300 mg/dose twice daily	Syrup well tolerated or can crush tablet. Can give with food. MUST WARN PARENTS ABOUT HYPERSENSITIVITY REACTION. ABC should be stopped permanently if hypersensitivity reaction.
Fixed-dose combination of ZDV plus 3TC plus ABC	No liquid available. Tablet: ZDV 300 mg plus 3TC 150 mg plus ABC 300 mg	Adolescents and adults	Maximum dose: >40 kg: 1 tablet/dose twice daily	Tablet cannot be split. MUST WARN PARENTS ABOUT HYPERSENSITIVITY REACTION. Abacavir should be stopped permanently if hypersensitivity reaction.
Non-Nucleoside reverse transcriptase inhibitors				
Nevirapine (NVP)	Oral suspension: 10 mg/ml Tablet: 200 mg	All ages	15 to 30 days: 5 mg/kg/dose once daily x 2 weeks, then 120 mg/m ² /dose twice daily x 2 weeks, then 200 mg/m ² /dose twice daily >30 days to 13 yrs: 120 mg/m ² /dose twice daily for 2 weeks, then 200 mg/m ² /dose twice daily Maximum dose: >13 yrs: 200 mg/dose once daily for first 2 weeks, then 200 mg/dose twice daily	If rifampicin coadministration, increase NVP dose by ~30%, or avoid use (see Tuberculosis section). Store suspension at room temperature; must shake well. Can give with food. MUST WARN PARENTS ABOUT RASH. Do not dose escalate if rash occurs (if mild/moderate rash, hold drug; when rash cleared, restart dosing from beginning of dose escalation; if severe rash, discontinue drug). Drug interactions.
Efavirenz (EFZ)	Syrup: 30 mg/ml (note: syrup requires higher doses than capsules, see dosing chart) Capsules: 50 mg, 100 mg, 200 mg	Only for children over 3 yrs	Capsule (liquid) dose for >3 yrs: 10 to 15 kg: 200 mg (270 mg = 9 ml) once daily. 15 to <20 kg: 250 mg (300 mg = 10 ml) once daily. 20 to <25 kg: 300 mg (360 mg = 12 ml) once daily. 25 to <33 kg: 350 mg (450 mg = 15 ml) once daily. 33 to <40 kg: 400 mg (510 mg = 17 ml) once daily. Maximum dose: ≥40 kg: 600 mg once daily.	Capsules may be opened and added to food but have very peppery taste; however, can mix with sweet foods or jam to disguise taste. Can give with food (but avoid after high fat meals which increase absorption by 50%). Best given at bedtime, especially first 2 weeks, to reduce central nervous system side effects. Drug interactions.
Protease inhibitors				
Nelfinavir (NFV)	Powder for oral suspension (mix with liquid): 200 mg per level teaspoon (50 mg per 1.25 ml scoop): 5 ml Tablet: 250 mg (tablets can be halved: can be crushed and added to food or dissolved in water).	All ages However, extensive pharmacokinetic variability in infants, with requirement for very high doses in infants <1 yr.	< 1 yr: 40-50 mg/kg/dose three times daily or 65-75 mg/kg/dose twice daily >1 yr to < 13 yrs: 55 to 65 mg/kg/dose twice daily Maximum dose: ≥13 yrs: 1,250 mg/dose twice daily	Powder is sweet, faintly bitter, but gritty and hard to dissolve; must be reconstituted immediately prior to administration in water, milk, formula, pudding, etc.—do not use acidic food or juice (increases bitter taste). Because of difficulties with use of powder, use of crushed tablets preferred (even for infants) if appropriate dose can be given. Powder and tablets can be stored at room temperature. Take with food. Drug interactions (less than ritonavir-containing protease inhibitors).
Lopinavir/ritonavir, (LPV/r)	Oral solution: 80mg/ml lopinavir plus 20 mg/ml ritonavir Capsules: 133.3 mg lopinavir plus 33.3 mg ritonavir	6 mos of age or older	>6 mos to 13 yrs: 225 mg/m ² LPV/57.5 mg/m ² ritonavir twice daily or weight-based dosing: 7-15 kg: 12mg/kg LPV/3 mg/kg ritonavir/dose twice daily 15-40 kg: 10 mg/kg lopinavir/5 mg/kg ritonavir twice daily Maximum dose: >40 kg: 400 mg LPV/100 mg ritonavir (3 capsules or 5 ml) twice daily	Preferably oral solution and capsules should be refrigerated; however, can store at room temperature up to 25° C (77° F) for 2 months. Liquid formulation has low volume but bitter taste. Preferably needs to be refrigerated. Capsules large. Should be taken with food. Drug interactions.

* Meter² body surface area calculation: square root of (height in centimeters times weight in kilograms divided by 3600).



IN THE LIFE



Alcides Troncoso

Vanity Fair readers have every month since 1993 enjoyed *The Proust Questionnaire*, a series of questions posed to celebrities and other famous subjects. The *Vanity Fair* questionnaire—modeled after a questionnaire Marcel Proust was asked to fill out in the late 1800s—reveals much about the respondents' lives, thoughts, values, and experiences.

In May 2002, *IAPAC Monthly* introduced "In the Life," through which IAPAC will feature members who have been asked to bare their souls through their answers to ten questions.

This month, *IAPAC Monthly* is proud to feature Alcides Troncoso, Head of the Infectious Diseases Unit at Francisco Muñiz Hospital in Buenos Aires, Argentina.

What proverb, colloquial expression, or quote best describes how you view the world and yourself in it?

The thought that has most influenced my life belongs to Albert Einstein: "Our times are sad times! It is easier to disintegrate an atom than a prejudice."

What activities, avocations, or hobbies interest you? Do you have a hidden talent?
Writing. One writes to avoid feeling unfortu-

nate. The art of writing is above all passion and pleasure. It is a dream, a conducted and deliberated dream, but fundamentally a dream. Somehow, all the poems from the past, the present, and the future, are fragments of one infinite poem written by all the poets of the world.

If you could live anywhere in the world, where would it be? Why?

I would live in Villa la Angostura, a town in the south of Argentina—a place known for the abundance of its wild landscape, its majestic mountains, its everlasting snow, the free running of its creeks, its marvelous lakes, the charming blossoming of its tulips, [and] the legendary strength of its winds. It is a sacred land of vast millenary cultures, which hides in its immensity the tutelary geniuses from a remote and unknown past and the inconsolable specter of the warrior shepherds, beaten and conquered, still carrying the seal of a race and tradition already extinguished.

Who are your mentors or real life heroes?

My hero, my archetype is Prometheus... His reward was a silent and intense suffering, the asphyxiating sensation of pain, the rock, the vulture and the chain – all of which mortifies dignity. But none of these was enough to make him show his agony. His divine crime was to alleviate human miseries and strengthen man's heart... for that he was [condemned] by Heaven. From his patient and energetic resistance and from the strength of his spirit, which Heaven and Earth could not break, leaves us a great learning. He is the symbol of undeserved suffering and willpower to resist oppression.

With what historical figure do you most identify?

Pasteur. Few physicians, if any, have had so much influence on the progress of medicine like a man who was not a physician, but a chemist: Louis Pasteur. He was an extraordinary investigator, sensible to the immediate experiences of his world and gifted with genius to find, at the same time, a quick scientific and pragmatic solution to problems.

Who is your favorite author, painter, and/or composer?

My favorite author is Oscar Wilde. The long centuries of literature offer us authors much more complex and imaginative than Wilde, but none of them more charming. He was charming in casual dialogue, in his friendship, in his years of happiness and adversity. He still is all that through each line he ever wrote. I believe that the virtue of charm is a

virtue without which all other virtues are futile. His work has not become old, it could have been written this morning.

If you could have chosen to live during any time period in human history, which would it be?

I would choose the Golden Century, between 1550 and 1650, a period that, as its name indicates, was the era of richness and light. Literature, painting, and all sorts of arts blossomed. It was the time of Cervantes and Shakespeare, and it was very special because all members of society chose to improve themselves by an honest introspection.

If you did not have the option of becoming a physician, what would you have likely become given the opportunity?

If I had not become a physician I would have become a gardener or perhaps a philosopher, in order to search for the answers to questions which, as men, pass us over, like the reason of pain and suffering, the reason of wickedness and death, etc.

In your opinion, what are the greatest achievements and failures of humanity?

The worst mistake of humanity of all times was the transformation of men into killer beasts, and the lack of mercy which originated and allowed the torture and infanticide of thousands of millions of innocent and defenseless children. This was the worst mistake, proving their strength on the weak, the worst form of cowardice. The greatest achievement was, without doubt, discovering vaccines and making them attainable to all to control epidemics.

What is your prediction as to the future of our planet one full decade from present day?

In this world pain is an inevitable reality. It grows alongside happiness, the same way we cannot stop a hurricane or silence a storm. Worse than feeling a great pain is not feeling at all... Notwithstanding, although it appears more logic to lack hope, I dream of a rainbow in a cloudy sky, a sunset in a gray afternoon. I hope that we do not lose our capacity of admiration for spirituality, that men resign hate and develop antibodies against the worst illness of our century, which is negative thinking. I hope for a more just society. Life is a great gift and a great asset, not for what it gives us, but for what it allows us to give to others and, paraphrasing Gandhi, there is sufficient richness in the world to satisfy the needs of all, but there is not sufficient richness to satiate the ambitions of some. ■



[Strength in Numbers]

[IAPAC Welcomes New and Renewing Members]

In May 2002, the International Association of Physicians in AIDS Care (IAPAC) welcomed 29 new and/or renewing dues-paying physician members from four countries. IAPAC thanks the following physicians for their support of the association's mission to improve the quality of care provided to all men, women, and children living with HIV/AIDS.

Andrew Badley, *Canada*
Richard Bax, *USA*
Richard Cazen, *USA*
David A. Cooper, *Australia*
Kathryn Crooks, *USA*

Edwin De Jesus, *USA*
Gerald Friedland, *USA*
Marc Gouretich, *USA*
Diane Havlir, *USA*
Kimberly Hines, *USA*
Joseph E. Hoagbin, *USA*
Nicholas Ifft, *USA*
Drew Kovach, *USA*
Stephen A. Lee, *USA*
Herbert Meyer Jr., *USA*
Esther Mwaikambo, *Tanzania*
James Oleske, *USA*
Linda Pacioretty, *USA*
Daniel Perlman, *USA*
Thomas Quinn, *USA*

Anita Rachlis, *Canada*
Eugene Rogolsky, *USA*
Philip Sanchez, *USA*
William Shay, *USA*
Bary Siegel, *USA*
Michael Stary, *USA*
Michael Steward, *USA*
John J. Sullivan, *USA*
James Witek, *USA*

To learn more about IAPAC individual physician and allied health professional membership, please contact Joey Atwell, Director of Membership, at (312) 795-4941 or jatwell@iapac.org.

[Recruit and Win]

Do you wish to strengthen the profession, enhance your colleagues' work, and win a prize? Your recruitment effort will not go unrecognized. Each time you recruit a new member, your name will be entered into a drawing to win one of the following prizes:

- One roundtrip, upgradeable, tourist class ticket anywhere United Airlines flies in the United States.
- One roundtrip, upgradeable, tourist class ticket anywhere United Airlines flies in Europe.

From March 1, 2002, to December 15, 2002, the more new members you recruit, the greater your chances of winning! Plus, you will receive recognition in the *IAPAC Monthly*.

Whether you sponsor one or 100 new members, you will receive a gift as recognition of your contribution to the success of this IAPAC membership campaign. There are four sponsorship levels; at the end of the campaign, you will receive a prize for the recruitment level you have met.

- Level 1 – Recruit one to four new members between March 1, 2002, and December 15, 2002, and receive an IAPAC lapel pin.
- Level 2 – Recruit five or more new members between March 1, 2002, and December 15, 2002, and receive an IAPAC lapel pin and a custom-designed plaque recognizing your commitment to IAPAC.

- Level 3 – Recruit 20 or more new members between March 1, 2002, and December 15, 2002, and receive Level 1 and 2 gifts and a 12-month complimentary extension of your IAPAC membership.
- Level 4 – Recruit 75 or more new members between March 1, 2002, and December 15, 2002, you may show off your accomplishment with a 10k yellow gold IAPAC lapel pin (and receive Level 2 and 3 gifts).

There is *Strength in Numbers*—encourage others to become IAPAC members. It is easy. To learn how easy, contact IAPAC's Membership Department at (312) 795-4941 or e-mail membership@iapac.org.

Rising to the challenge

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to be given to providing technical assistance at the local level in order to better determine what are the ongoing and changing priorities in each case. In aggregate, this would enable national and local authorities to truly become full partners in the processes that determine how the funds for which they are applying, are best spent. As projects are chosen and as funds are earmarked, what remains most important is that governments faced with the incessant misery of public despair and death be able to execute programs to improve the quality of life of their citizens, espousing at base a single key message: "You have the right to live."

Although the existence of complacency on the part of certain governments throughout the world remains an unfortunate reality, most governments demonstrate passionate commitment to a balanced regimen of disease prevention and treatment. Lesotho's Prime Minister, Pakalitha B. Mosili, for example, speaks fervently of prevention as a first line of defense. Yet, in the same breath, he urges that, "we need to improve access to quality care and support..."

Adding to this call for a balanced approach to prevention and treatment of HIV/AIDS is a veritable roll call of world leaders:

- Vietnam's Deputy Prime Minister Pham Gia Khiem:

"We need to enhance the quality of care for infected people, support research on HIV/AIDS, and ensure adequate access to necessary medications and their affordability to the population."

- Peru's President Alejandro Toledo:

"We expect to have to face up to [promoting] solidarity and support for people affected by the epidemic, to give them better access to healthcare and lower costs for medicines, special tests and examinations, not forgetting antiretroviral treatments."

- Jamaica's Prime Minister Percival James Patterson:

"We need a comprehensive strategic plan [that takes] into account prevention, education, behavioral changes, communication, and appropriate care and support for people living with HIV/AIDS."

Clearly, there is a keen appreciation by the custodians of the world's most affected populations that a balance must be struck in our funding and policy efforts. They know, as do the vast majority of us engaged in this battle, that prevention and treatment work in positive synergy.

A poignant reminder of this fact is further illustrated by Botswana's President, Festus G. Mogae, when he tells us that, "Some children are 14 or 15 years old when their parents die. If their parents' lives could be prolonged for another five to six years, it would be better than their leaving their children orphans at that young age." It is far from exaggeration to suggest that if treatment is not assured, we will be resigning our future to a world of orphans, torn from the care, guidance, and support of the family structure. Bereft of such support systems, one must wonder at the extent to which any form of prevention activity will truly be capable of reaching these adults of tomorrow. And so, if long-term sustainability is what we seek, then we must quickly come to appreciate and act upon this need to balance the scales of our funding.

As we move on to subsequent rounds of funding, the opportunity to heed the lessons of the present becomes our greatest asset. Of promise in this regard is the appointment of IAPAC member Richard Feachem (currently Director of the Institute of Global Health at the University of California, San Francisco) to serve as the GFATM's Executive Director effective July 2002. This appointment leads IAPAC to look to the future with both hope and raised expectations. Toward the end of ensuring that the GFATM will produce the results of which such sums are clearly capable, IAPAC looks forward to working closely with the GFATM's leadership, wherever possible, in order to bring to bear the knowledge and commitment of our association.

Further, and in support of recent calls by several international health bodies, IAPAC supports a global campaign meant to replenish the GFATM's coffers and, as important, to subsidize developmental activities meant to address parallel epidemics of poverty and isolation. While the GFATM is an impressive first step toward adequate funding for major international public health concerns, the reality is that these levels continue to fall short of what health economists, such as Columbia University's

Jeffrey Sachs, calculate are required to both combat major epidemics and restore financial solvency to the world's resource-limited nations.

As a signpost in this regard, precise targets have been provided by the World Health Organization (WHO), whose recent report, *Macroeconomics and Health: Investing in Health for Economic Development*, states that, "by 2015-2020, increased health investments of [US]\$66 billion annually above current spending will generate at least [US]\$360 billion while saving 8 million lives a year." With this goal in mind, and with a clear plan for future spending increases having already been tabled by the WHO's Commission on Macroeconomics and Health, it is time for us to work together to scale up the GFATM in further service of the world's embattled citizens.

A report published in last month's issue of the *IAPAC Monthly* exposed the fact that governments had pledged no more than US\$1.8 billion to the GFATM as of May 2002. And, contributions from the private sector are equally disappointing, with the notable exception of the Bill & Melinda Gates Foundation's US\$100 million contribution announced almost a year ago. There is no excuse for the most affluent countries of the world (otherwise known as the G7), as well as the private sector (among which are multinational companies, many of whose annual operating budgets equal some developing world countries' annual economies), to doom the GFATM to failure by pinching their collective pennies. There is a biblical allusion that comes to mind as I contemplate this state of affairs—"For what shall it profit a man, if he shall gain the whole world, and lose his own soul?"

We are now faced with a unique and unparalleled opportunity to crush the tide of HIV/AIDS. While the unfortunate and irreversible reality is that millions of human lives have been lost in the time that it has taken to harness the collective will and resources that are finally represented in the form of the GFATM, its existence, as well as our lessons from the first round of distributions, now afford us the opportunity to redeem ourselves. May we all rise to the challenge. ■

José M. Zuniga is President of the International Association of Physicians in AIDS Care and Editor-in-Chief of the IAPAC Monthly.



SAY ANYTHING

The highest priority in the early days is for the [GFATM] to demonstrate impact and effectiveness on the ground. The [GFATM] has clearly not been established as a research-funding agency. However, applied and operational research will be essential to facilitate and improve effectiveness.

Richard Feachem, newly appointed Executive Director of the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM), quoted in the May 4, 2002, issue of The Lancet. Feachem, who has served as the World Bank's senior professional in the health sector and is a former Dean of the London School of Hygiene and Tropical Medicine, accepted to head the GFATM at an extremely challenging juncture. In April 2002, the GFATM Board effectively disbursed US\$1.6 billion of the US\$1.9 billion at its disposal. Since its launch, financial contributions to the GFATM have decreased significantly in recent months, and are far below the originally intended level.

Teenagers who were at school during the AIDS awareness campaigns of the 1980s are now adults, but today's teenagers are much less aware of the facts—a survey last year found that 40 percent of 11-year-old boys had never heard of HIV.

Nick Partridge, Chief Executive of the UK-based Terrence Higgins Trust, in a May 7, 2002, BBC News report. Partridge said that according to new research from Datamonitors, teenagers in the United Kingdom think of AIDS as something that will not affect them. According to Dheeraj Khiytani, an HIV analyst at Datamonitors, people under age 30 are particularly vulnerable and live a lifestyle "almost in ignorance of the threat of AIDS."



IAPAC Senior Vice President/Chief of Staff Michael S. Glass (left, with back to camera) briefs a delegation of physicians and public health officials from China visiting the IAPAC Headquarters in April 2002. The delegation wished to learn about the development and implementation of prevention and care activities worldwide as part of their efforts to craft China's response to HIV disease.

We think that the inability of health departments to get in touch with and work with the people who are infected misses a great opportunity to prevent further transmission.

Ron Hattis, Secretary-Treasurer of Physicians for HIV Control, in a May 4, 2002, Associated Press report entitled, "Doctors, Labs for First Time Have to Report New HIV Cases." Hattis's organization opposes a California requirement that beginning July 1, 2002, physicians and laboratories in California report newly diagnosed HIV cases to state public health officials utilizing numerical codes rather than names. According to the Associated Press, the reporting requirement differs from 33 other states that track patients by name, and will differ from how California tracks 80 other diseases. Only Illinois, Kentucky, Maryland, Massachusetts, Vermont, and Puerto Rico currently use numerical codes instead of names. In 1998, the US Centers for Disease Control and Prevention (CDC) asked states to track HIV infection as an integral part of AIDS reporting programs, urging individuals be identified by name but allowing states to use codes.

Generic competition is the way forward. If we have generics at a fair price, then the majority of these people will be able to see their next birthday. Or see their children finish school.

John Wasonga, a Kenyan physician, reacting to a law that went into effect May 1, 2002, allowing generic and other inexpensive antiretroviral drugs to be imported into Kenya and/or manufactured in the country. BBC Online reported that only 3,000 of an estimated 2 million Kenyans living with HIV/AIDS are now on antiretroviral therapy, which costs about US\$85/month per patient. GlaxoSmithKline Kenya Marketing Director William Kiarie argues "bringing the price down by 10 percent, 20 percent, we are going to see very little increase in people using [antiretroviral] drugs. Basically because people are poor, and governments are poor."



Look to the August and September 2002 issues of *IAPAC Monthly* for coverage of the XIV International AIDS Conference, which will be held July 7-12, 2002, in Barcelona.