This technical brief is designed to provide key technical information to guide proposal development and ensure that proposals include antiretroviral treatment (ART) in comprehensive HIV care and treatment services. The prevention and assessment of HIV drug resistance (HIV DR) and pharmacovigilance are covered superficially as those topics are covered in separate technical guidance notes.

Rationale for including the SDA in the proposal

The proposal will need to provide justification for why ART is important to reduce mortality, morbidity, orphan hood and preserve families, and should also link to other relevant national goals or targets, such as the Millennium Development Goals. The proposal may be used to augment existing programme activities outlined in the national strategy or may be designed to add new programme activities, such as the prevention and assessment of HIV drug resistance, pharmacovigilance, or expansion of access to first-line and second-line therapies. Infants, children and pregnant women are currently underrepresented in many treatment programmes, and in some countries other groups may need to be a focus for a country proposal, e.g., infants, TB patients or injecting drug users (IDUs). To maintain the effectiveness of first-line and second-line therapies, standardized simplified national guidelines for ART are recommended for use in public and private (for and not for profit) sector and activities to support prevention and assessment of HIVDR are recommended. Pharmacovigilance activities are also important to monitor and capture short and long term adverse events and toxicities related to ARV and other drugs used in HIV treatment and improve programme outcomes.

Elements to be considered in the situation analysis

- Number of adult and children living with HIV
- Number of HIV related deaths in a year
- Number of adults and children in need of ART
- Coverage of ART services (disaggregated by sex, age and other vulnerable groups, urban and rural distribution)
- Number and level of health facilities providing ART and HIV care

Examples of programme objectives

To increase coverage of antiretroviral treatment for adult and children living with HIV who need it from xx% to yy%.
To increase access for X population to second line ART
To increase access for infants/children or pregnant women or other group living with HIV to ART
To increase access of pregnant women to ART and prevent MTCT transmission
To promote active surveillance for ARV adverse events and toxicities
To develop and implement national strategy for HIV DR prevention and assessment
Target populations

Target population for ART:
- Adults and children currently on ART (continue treatment)
- Adults and children newly diagnosed with HIV and known to be eligible for ART, but not on ART
- Estimated number of adults or children diagnosed with HIV but not yet referred or attending HIV care

National guidelines should explicitly specify eligibility criteria, specify standard regimens and options for specific target groups such as patients with active TB or liver disease and be supported by a limited national formulary.

The number of people requiring ART can be estimated by using the Spectrum HPP statistical package, taking into account the prevalence of HIV infection, HIV related mortality and national population. In providing of ART special attention needs to be paid to children, women, TB patients and IDUs and other hard to reach groups locally identified.

Suggested activities

1. **Review and update guidelines if necessary**
   - Treatment guidelines need reviewed from time to time in the light of new evidence, programmatic experience and consistency with current WHO ARV treatment guidelines. The WHO ART guidelines for **adults and adolescents** were updated in 2010. WHO now recommends an earlier start to treatment for all HIV-infected individuals with a CD4-cell count of 350 cells/mm3 or less and those with advanced HIV clinical disease, active tuberculosis, or active chronic hepatitis B irrespective of CD4-cell count. They are based on evidence of both individual and public health benefits of starting treatment earlier. Countries are also urged to move away from the least costly but more toxic regimens that contain stavudine to regimens that contain zidovudine or tenofovir for all patients starting lifelong therapy. The recommendations also emphasize the importance of fixed-dose combinations and outline an expanded role for laboratory monitoring of both CD4 and viral load, to improve the quality of HIV treatment and care. Access to these laboratory tests is not, however, a prerequisite for treatment. (See: [Rapid advice: antiretroviral therapy for HIV infection in adults and adolescents.](http://www.who.int/hiv/pub/arv/advice/en/index.html))
   - Revised ART treatment recommendations for infants and children were released summary format on 16 June 2010, and will likely be released in full before the end of July 2010. It is now recommended that all infants diagnosed with HIV need to immediately start ART. All HIV exposed infants need virological testing at or around 4-6 weeks of age to detect HIV early. Infants with HIV who have NOT received nevirapine as prophylaxis at or around birth should start on a nevirapine based first line regimen; and infants with HIV who have received nevirapine as prophylaxis should start ART with a lopinavir/ritonavir containing treatment regimen. The summary of the new recommendations can be found on [http://www.who.int/hiv/pub/paediatric/paed_prelim_summary/en/index.html](http://www.who.int/hiv/pub/paediatric/paed_prelim_summary/en/index.html).
   - Readers are encouraged to check the WHO HIV/AIDS department website (www.who.int/hiv/en) for the full update prior to finalizing their applications.
   - Nutritional support for infants and their families may be required (see also SDA on nutrition). See: [Rapid advice: infant feeding in the context of HIV](http://www.who.int/hiv/pub/paediatric/advice/en/index.html)
• **Pregnant Women.** Pregnant women either need ART if eligible or combination preventive MTCT ARV regimens as outlined in the new WHO ART guidelines for adults and additional recommendations were established in the PMTCT guidelines updated in 2010. For HIV-infected pregnant women, the changes emphasize the crucial role of CD4 testing in identifying those who are in need of antiretroviral therapy and at greatest risk of transmission, coupled with earlier and more efficacious antiretroviral prophylaxis options, including triple combinations. For women known to be HIV-positive and intending to breastfeed, extended antiretroviral prophylaxis for mother and infant throughout the breastfeeding. See Rapid advice: use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants [](http://www.who.int/hiv/pub/mtct/advice/en/index.html)

• **TB patients.** HIV infected individuals with active TB disease should start ART irrespective of CD4 cell count and as soon as possible after initiation of TB treatment. Co-treatment for HIV TB frequently may require modification of ART regimens; usually the preferred NNRTI is efavirenz. Rifampicin has significant drug interactions with protease inhibitors and all protease inhibitors in standard doses are contraindicated. However, lopinavir and saquinavir may be used with an adjusted superboosted dose of ritonavir or doubling the daily standard dose of lopinavir.

• **Injecting drug users. Hepatitis B and C are common.** Patients with HIV/HBV co-infection that need concomitant therapy, should use an ART regimen with 3TC or FTC and TDF wherever possible, as 3TC, FTC and TDF have both anti-HIV and anti-HBV activity.

2. **Build human capacity through training**

A key tenet of the WHO public health approach to ART and HIV care is to increase capacity to deliver ART is through integrated and decentralized service delivery. The Integrated Management of Adolescent and Adult Illnesses (IMAI) is a series of tools proposed by WHO to develop clinical service at lower levels of the health care system in resource limited settings. IMAI integrates simplified clinical management of HIV/AIDS (with back-up from clinical mentors and referral to hospital) into the routine work of existing health services with strong community linkages. It covers the range of HIV/AIDS-related prevention, care and treatment issue, and supports a district network model, with back-up for services provided at health centre and district hospital level by clinical mentors within a strengthened consultative/referral and back-referral system.

IMAI strengthens services at the level of communities, health centres and hospitals and is implemented according to a strategy with a carefully organized sequence of steps: introduction and orientation, country adaptation, courses for district managers, training of trainers, sustained training support and supervision, emergency introduction to pre-service health-worker training programmes, etc. Additional tools and support is available at: [http://www.who.int/hiv/capacity/en/index.html](http://www.who.int/hiv/capacity/en/index.html)

3. **Improve access to drugs & diagnostics**

Access to HIV drugs and diagnostics is supported by WHO and close to 20 partners in the AIDS Medicines and Diagnostics Services (AMDS). Essential information is made available through its Global Price Reporting Mechanism - which list and benchmarks prices of antiretrovirals, HIV diagnostics, TB drugs and malaria drugs. It also provides access to procurement information for opioid substitution therapy and oral morphine, and links to quality information about the drugs concerned (the WHO prequalification program and US FDA pre-approval process). Logistics and supply management are supported by the partner organizations in the network, which can be contacted via the AMDS website. For more info: see [http://www.who.int/hiv/amds/en/](http://www.who.int/hiv/amds/en/)
4. **Strengthen patient retention and adherence**

Adherence to ART is an essential component of individual and programmatic treatment success. Programmes may seek to use global fund proposals to build in activities to promote and support patient retention and adherence. Programme elements that may be required include:

- Use of fixed dose combinations as preferred options in drug formularies
- Adherence counseling
- Subsidy or removal of user fees
- Development of people living with HIV as expert patients and community treatment supporters.
- Adherence support tools for patient groups (children, care givers, adults), eg, diaries, pillboxes, reminder systems
- Pharmacy refill measures (ARV drug pick-up pharmacy registers or dispensing records)
- Modified strategies for directly observed therapy/ or supported therapy for specific groups such as, prisoners, infants, pregnant women

WHO can provide tools and protocols such as IMAI, IMCI.

5. **HIV Drug Resistance Prevention and Assessment**

The emergence of HIV drug resistance (HIVDR) is inevitable, given HIV’s high replication and mutation rates and the necessity for lifelong antiretroviral treatment (ART). To maintain the effectiveness of first- and second-line ARV regimens, WHO recommends that countries develop a national strategy for HIVDR prevention and assessment. The recommended strategy was developed in consultation with WHO HIVResNet, a global network of specialists and institutions. Technical assistance is available to countries from the WHO HIV Drug Resistance Team and from other specialists in the network. WHO also provides protocols and tools on request, also please see [http://www.who.int/hiv/drugresistance/en/index.html](http://www.who.int/hiv/drugresistance/en/index.html)

The WHO-recommended strategy includes the following elements:

- Development of a national HIVDR Working Group, five year plan and budget
- Regular assessment of HIVDR “early warning” indicators from all antiretroviral treatment (ART) sites or representative sites
- Surveys to monitor HIV drug resistance prevention and associated factors in ART sites
- HIVDR transmission threshold surveys where ART has been widespread for ≥ 3 years
- HIVDR database development
- Designation of an in-country or regional WHO-accredited HIVDR genotyping laboratory
- Review of and support for HIVDR prevention activities
- Preparation of annual HIVDR report and recommendations for ART and prevention planning

Also see the Technical brief on HIVDR in this toolkit.

6. **Strengthen pharmacovigilance systems**

The effectiveness of treatment programmes, particularly in low and middle income countries, risks being compromised by problems related to toxicity, intolerance and drug-drug interactions. These adverse events, be they acute or chronic, mild or serious, are relatively common phenomena affecting both individual patients and public health, but are being only intermittently identified and scarcely reported in low and middle income settings. In strengthening pharmacovigilance (PV) for ARVs (ARV/PV) countries should consider the following:

- Situation assessment. Including mapping of existing and type of activities related to ARV/PV as well as evaluation of needs.
- Develop or review national plans. Where there is no pre-established PV system in the country: consider establishing beginning with few sentinel sites.
- Train health workers in pharmacovigilance.
- Develop or review national guidelines on adverse effects of ARV drugs.
- Establish a national expert working group on pharmacovigilance
- Establish linkages with the International Drug Monitoring Centre
Approach to costing these activities

A number of tools for costing antiretroviral treatment are available. They include the following:

- The WHO Workplanning and Budgeting Tool, which helps countries develop a costed workplan and budget for Global Fund proposals.
- The WHO HIV/AIDS Unit Cost Calculator helps countries calculate unit costs of various HIV/AIDS interventions.
- The Resource Needs Model, developed by the Futures Institute, estimates overall resource needs for most interventions.
- The Activity Based Costing (ABC) model, developed for the AIDS Strategic and Action Plan (ASAP) mechanism, helps countries cost operational plans.
- The Clinton HIV AIDS initiative also has costing tools for paediatric HIV treatment.

For the purposes of developing a Global Fund proposal budget, WHO recommends using the Workplanning and Budgeting Tool, which is available at [http://www.who.int/hiv/pub/toolkits/GF-Resourcekit/en/index2.html](http://www.who.int/hiv/pub/toolkits/GF-Resourcekit/en/index2.html).

Suggested key indicators

Note that existing indicators used in national programmes should be used wherever possible, but specific modifications to ensure services for children are tracked are recommended. Specific indicators for HIV DR and pharmacovigilance are described elsewhere.

<table>
<thead>
<tr>
<th>Availability</th>
<th>Coverage</th>
<th>Outcome/Impact</th>
</tr>
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<tbody>
<tr>
<td>Existence of updated national policies ad guidelines in line with international standards</td>
<td>Percentage of adults with advanced HIV infection receiving antiretroviral therapy</td>
<td>Percentage of adults and children with HIV still alive and known to be on treatment 12 months after initiation of antiretroviral therapy</td>
</tr>
<tr>
<td>Percentage of health facilities that offer ART (i.e. prescribe and/or provide clinical follow-up)</td>
<td>Percentage of infants with HIV receiving ART</td>
<td>Percentage of individuals who are still on treatment and who are still prescribed a standard first-line regimen after 12 months from the initiation of treatment</td>
</tr>
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| Percentage of children (under 15 or locally defined) with advanced HIV receiving ART |

Linkages with other interventions/programmes

Delivery of antiretroviral treatment requires effective linkages with the following programmes/services:

- TB, viral hepatitis, VCT, and PMTCT programmes
- Maternal and Child health/IMCI/infant and young child feeding
- Immunization
- Nutrition
- National reference laboratory
- Essential medicines
- Community health programmes
- Pharmacovigilance.

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1 The Inter Agency task team (IATT) for PMTCT has been working with all IATT partners to improve guidance on programme monitoring and includes additional indicators that address children. These can be obtained from WHO or UNICEF (Priscilla Akpama pakwara@unicef.org or Chika Hayashi hayashic@who.int).
Addressing gender, human rights and equity

Antiretroviral treatment needs to be made available and accessible to all people who need it, without discrimination. User fees for any portion of ART services, including patient monitoring adversely impact uptake adherence and success of programmes, particularly for poor and other vulnerable populations. Particular attention needs to be paid to reaching and sustaining treatment among:
- Infants and children
- Poorest and rural families
- Young mothers
- Family HIV care
- IDU
- Migrants and refugees
- Prisoners

Key implementing partners to be considered

- Providers of ART services, including public sector, NGO/FBO and private sector
- National child and maternal health programmes
- Actors in the national drug supply chain management system
- PMTCT programmes
- PEPFAR implementers
- Other development partners (UNITAID, Clinton HIV AIDS Initiative, Baylor University, MSF)
- UN partners (WHO, UNICEF, UNAIDS, UNFPA)

Type and sources of technical assistance which might be required during implementation

Areas in which technical assistance might be required include the following:
- Strengthen drug procurement and supply chain management systems
- Laboratory services, including implementation of mechanisms to allow for point of care technologies and dried blood spots
- Estimation and forecasting for national requirements for ART
- Development/revision of national policy and technical guidance documents, including dosing guidance for practitioners
- Developing implementation plans
- Developing programme activities to support monitoring and quality improvement
- Development and implementation of training, supervision and mentoring
- HIV Drug Resistance Prevention and Assessment
- Pharmacovigilance