HIV DRUG RESISTANCE
FACT SHEET, APRIL 2011

Key facts

- Rates of transmitted HIV drug resistance* continue to remain limited in low- and middle-income countries, according to the initial survey findings by WHO. A combined analysis of all surveys conducted in 20 countries showed an overall transmitted drug resistance rate of 3.7% (95% Confidence Intervals 2.86-4.54).

- The WHO surveys of transmitted HIV drug resistance were conducted in 41 areas: 75% in Africa (31 surveys), 22% in Asia (9 surveys) and one in Mexico. Over 1,900 people, who had been recently infected with HIV and had not received treatment, were enrolled in the surveys between 2003 and 2009.

- Eighty-three per cent of the surveys showed resistance levels less than 5%, a "low" level in particular if compared to the rates of 10% - 20% reported in Europe and the United States. However, 17% of surveys showed levels of 5-15%, classified as a "moderate" level. Results highlight the need for further surveillance and monitoring.

- From 2007–2010, WHO also conducted 15 surveys of acquired HIV drug resistance* at clinics in Burundi, India, Malawi, Mozambique and Nigeria.

- The surveys showed that, of 2,150 patients initiating antiretroviral therapy (ART) at these clinics, 6% had baseline drug resistance to any antiretroviral drug. Some of these patients had previously been exposed to antiretroviral drugs, either for prevention of mother-to-child transmission (PMTCT) or for their own health at 12 months.

- Of the patients who were still alive and in care after 12 months, 90% had viral loads below 1,000 c/ml similar to cohorts in developed countries. Of the remaining 10% of patients with viral loads greater than 1,000 c/ml, two-thirds showed resistance to any antiretroviral drug. Observed resistance patterns suggest that second line treatment options are likely to be effective for the majority of patients failing first line therapy.

- These results suggest that if virological monitoring were to be made routinely available, treatment failure could be identified at an early stage and patients offered effective second-line treatment. Earlier start of a second-line regimen after failure of first-line options can help patients avoid accumulation of drug resistance mutations and preserve efficacy of their second-line treatment.

- Overall, the WHO surveys confirm that HIV drug resistance rates remain limited, despite the initial fears of some experts that massive scale-up of HIV treatment in developing countries would lead to widespread problems.
During 2006-2010, 102 surveys of HIV drug resistance Early Warning Indicators were completed in 52 countries, covering 66,851 patients in more than 2,100 clinics. Data suggest that adherence, drug stock-out, and lost to follow-up were problematic, requiring particular attention and continuous monitoring.

What is HIV drug resistance?

Over the past decade, access to ART for HIV has dramatically increased in low- and middle-income countries. From preliminary data, more than 6 million people were receiving ART in these countries at the end of 2010, as compared to just 400,000 at the end of 2003.

HIV drug resistance refers to the ability of the virus to withstand the effects of a given antiretroviral drug to prevent its replication. Drug resistant virus will continue to replicate in the presence of the drug to which it has become resistant.

As ART continues to expand, the emergence of some drug resistance is inevitable. Insufficient knowledge among patients and health workers, suboptimal adherence to treatment regimens, drug stock-outs, and inadequate patient monitoring mechanisms, are among the many factors leading to treatment failure and eventually drug resistance.

If patients develop HIV drug resistance to their first-line regimen, they stop responding to it effectively. In order to stay healthy, they need to receive a second-line regimen. In 2010, in low- and middle-income countries, second-line treatment regimens were on average at least six times more expensive than first-line treatment. Keeping drug resistance at bay is therefore a key strategy to the success and sustainability of HIV treatment programmes.

Table 1. Prices for two of the most commonly used WHO-recommended antiretroviral drug regimens in low- and middle-income countries, 2010

<table>
<thead>
<tr>
<th>First-line treatment</th>
<th>Second-line treatment</th>
</tr>
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<tbody>
<tr>
<td>3TC+NVP+ZDV [150+200+300]mg</td>
<td>ZDV+ddl+[LPV/r] 300mg+400mg+[200+50]mg</td>
</tr>
<tr>
<td>EFV+[3TC+ZDV] 600mg+[150+300]mg</td>
<td>ABC+ddl+[LPV/r] 300mg+400mg+[200+50]mg</td>
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Source: Global Price Reporting Mechanism Report, March 2011, AIDS Medicines and Diagnostics Service, WHO

What is WHO doing to control HIV drug resistance?

WHO has been at the forefront of the global campaign to scale up life-saving antiretroviral treatment in low- and middle-income countries. It has also led efforts to assess HIV drug resistance at the population level, using standardized methods that allow for comparison of results over time and across regions.
In 2004, WHO developed a Global Strategy for the Prevention and Assessment of HIV Drug Resistance. The Strategy aimed to:

- Inform the selection of first- and second-line regimens for ART, as well as antiretroviral drugs for PMTCT, at population level
- Support national HIV programmes in minimizing the emergence and transmission of HIV drug resistance.

At the global level, WHO has established the HIVResNet, a network of over 50 institutions, laboratories and experts, to support capacity building, surveillance and data analysis.

WHO has provided countries with "Early Warning Indicators" guidance and tools—a set of indicators to monitor the functioning of ART sites and minimize the emergence of drug resistance, using information collected routinely from medical and pharmacy records.

A global network of laboratories has been created and now expanded to over 60 laboratories that are either accredited by WHO for HIV drug resistance testing, or applied for such accreditation. Two thirds of these laboratories are located in Africa and Asia.

WHO urges countries to establish and strengthen their strategies to assess and prevent HIV drug resistance as an essential step towards improving the efficiency of HIV treatment programmes. Around 50 countries have developed national HIV drug resistance working groups and strategies to monitor the emergence and transmission of HIV drug resistance.

Figure 1. Network of HIV drug resistance laboratories, 2011

Source: Silvia Bertagnolio et al. WHO presentation delivered at the 18th Conference on Retroviruses and Opportunistic Infections "Surveys of transmitted and acquired HIV drug resistance in resource-limited settings", February 2011
What should be done in the future?

- Despite these overall positive findings on low rates of HIV drug resistance, countries and clinical sites should continue to ensure routine, standardized and population-based surveillance of HIV drug resistance. This is essential in order to avoid the further emergence of drug resistance, which has the potential to severely undermine efforts to extend life-saving HIV treatment to millions of people.

- National HIV drug resistance assessment strategies should be developed and routinely implemented as part of comprehensive HIV treatment programmes. Partners and donor organizations must step up their support to help countries develop and sustain population-based HIV drug resistance efforts.

- In 2010, WHO and UNAIDS launched the "Treatment 2.0" initiative to catalyze the next phase of ART in developing countries, with more optimized, affordable and efficacious regimens, which will help patients improve treatment adherence and avoid drug resistance.

* HIV drug resistance* may be transmitted or acquired. Patients could develop drug resistance, if their treatment was interrupted or not taken according to prescription. This phenomenon is called **acquired drug resistance**. If people are infected by others who had HIV drug resistance, it is called **transmitted drug resistance**.

**HIVDR Early Warning Indicators** are standardized tools for programs and sites to assess performance in minimizing situations which favour the emergence and transmission of HIVDR.