

## **Two Cipla AIDS Drugs Removed from WHO Prequalification List**

In 2001, the United Nations started a pilot project to assess the quality of malaria, TB and HIV/AIDS pharmaceutical products that the UN agencies (WHO, UNICEF, UNFPA and UNAIDS, supported by the World Bank) purchase. Managed by the World Health Organization, the Prequalification Project assesses essential medicines and their production sites worldwide based on dossiers submitted by drug manufacturers.

The WHO Prequalification Project has so far assessed more than 90 drugs, over half of these generics. The existence of an international system of prequalified products has dramatically increased access to essential medicines, particularly antiretroviral drugs, in developing countries. The list is updated regularly and it provides vital guidance for governments in procuring essential drugs which meet internationally-agreed quality standards.

On May 27<sup>th</sup> 2004, the WHO removed two products from its prequalification list. The products are two antiretroviral medicines manufactured by the Indian company Cipla: lamivudine (3TC) 150 mg tablet (LAMIVIR®), and the fixed dose combination lamivudine (3TC) 150mg/zidovudine (AZT) 300mg tablet (DUOVIR®)<sup>1</sup>.

### ***How could products have been prequalified and later withdrawn from the list?***

The WHO prequalification project is an ongoing process that includes periodic inspections of production sites and pharmaceutical company sub-contractors.

These two products were taken off the list because of questions concerning a bioequivalence study, one element of the dossier submitted to WHO by Cipla. As is standard practice in the industry, Cipla commissioned a Contract Research Organization (CRO) to conduct the bioequivalence studies for these products in 2001.

Initially, the studies conducted by this CRO were accepted by WHO, based on documentation submitted. However, a recent inspection by WHO of the CRO showed that there were deficiencies at this organization and, as a result, previously accepted studies and data are now considered inadequate.

---

<sup>1</sup> The WHO decision does not affect Cipla's triple fixed-dose combination nevirapine/lamivudine/stavudine (TRIOMUNE), which is still on the prequalification list, or any other Cipla products.

Therefore the two products have been removed from the prequalification list<sup>2</sup>.

WHO has informed Cipla and the CRO of the outcome of the inspection. If Cipla submits new data, these will be assessed and the products could be again considered for inclusion on the prequalification list, if the data are found acceptable.

**The manufacturing sites and the quality of these two products are not being questioned by the WHO. Rather, in the recent inspection, the CRO that conducted the bioequivalence studies was found to have failed to meet international standards, leading to lack of proof of therapeutic equivalence.**

MSF supports the WHO Prequalification Project and believes that ongoing monitoring by the WHO is a sign of an efficient process. The rigour of this process ensures that companies are always striving to improve their assessment of quality.

### **Cipla communications**

Cipla has informed MSF that if countries or organizations prefer to return these two products rather than continue using them, Cipla will offer full refunds. Cipla has also confirmed it has already began new bioequivalence studies on the two products and that these studies will be completed by the end of July.

### **MSF's response**

MSF's first priority is to ensure that no patients in our programmes face treatment interruption. MSF also recognizes that the ultimate authority for decisions on the use of drugs rests with a country's national drug regulatory authority (NDRA).

Considering these two points, MSF has decided to put supplies of these two Cipla drugs on hold until the results of new bioequivalency studies are available and are reviewed by the WHO Prequalification Project.

In general, MSF will seek to substitute other prequalified drugs for the two Cipla drugs, but the use of these two products will be decided on a case-by-case basis taking into consideration the decisions of NDRAs and availability of alternatives.

Since the vast majority of MSF's patients are on triple fixed-dose combinations, they will not be affected.

---

<sup>2</sup> The WHO has posted the following explanation on their website (May 27<sup>th</sup> 2004):

"[the two products were] Removed from the list as a result of the outcome of an inspection performed by the World Health Organization (WHO) in which compliance with Good Clinical Practices (GCP) and Good Laboratory Practices (GLP) was assessed, as well as data verification of the bioequivalence study at the Contract Research Organization (CRO) used by the sponsor. Products are subject to re-assessment when completely new data set is presented about the bioequivalence studies."