

**8th Invitation to manufacturers of medicinal products
for HIV and related diseases
to submit an Expression of Interest (EOI) for product evaluation to the
WHO Prequalification of Medicines Programme**
(August 2008)

To support national and global efforts to increase access to and the affordability of HIV/AIDS-related care and treatment, WHO, together with UNICEF, UNAIDS and UNITAID, invite manufacturers of selected pharmaceutical products to submit **Expressions of Interest (EOIs)** for product evaluation. The first Invitation to EOI for products for HIV/AIDS-related care and treatment was published in 2000 and the 7th Invitation was published in May 2007.

Article 1. Procedure for this Invitation to EOI

The current Invitation is published in accordance with the *Procedure for assessing the acceptability, in principle, of pharmaceutical products for purchase by United Nations agencies*, adopted in 2001 by the 37th WHO Expert Committee on Specifications for Pharmaceutical Preparations, and amended subsequently as part of the 41st report of the Committee, published as [No. 943 of the WHO Technical Report Series](#) in 2007.

Assessment of product(s) submitted under this Invitation will include evaluation of :

- product dossiers, which must include product data and information as specified in the [guidelines for submission](#)
- manufacturing sites, which must adhere to [good manufacturing practices](#) (GMP)
- clinical sites (if applicable), which must adhere to [good clinical practices](#) (GCP).

If evaluation demonstrates that a product and its corresponding manufacturing (and clinical) site(s) meet WHO recommended standards, it will be included in the [list](#) of medicinal products that are considered to be acceptable for procurement by UN organizations and others.

Article 2. Medicinal products included on the 8th Invitation

The ultimate aim of this 8th Invitation is to increase the range of selected products and sources available in relation to treatment for HIV/AIDS. The medicines listed in the 8th Invitation have been identified by WHO Department of HIV/AIDS as vital to effective treatment for people living with HIV/AIDS. These products are included either in the [WHO Model List of Essential Medicines](#) and/or in the [WHO treatment guidelines relating to antiretroviral therapy for HIV infection in adults and adolescents](#), and [in infants and children](#).

Products included in the WHO Model List of Essential Medicines are those which satisfy the priority health care needs of a population. They are selected on the basis of disease prevalence, evidence on efficacy and safety, and comparative cost-effectiveness.

Products included in WHO treatment guidelines are selected on the basis of an assessment of the quality of evidence for benefits, harms, costs, and appropriateness for use in a variety of situations, taking into account needs of special populations, and the values and preferences of the groups (professional and patient) using them.

Interested manufacturers are encouraged to submit documentation for recommended dosage forms and strengths, as specified below, of medicinal products in the following categories. Appropriate solid dosage formulations should be scored for pediatric use purposes and relevant evidence should be provided to support equal distribution of active ingredients in the scored products, especially in case of fixed-dose combination products. Products added to the 8th Invitation are highlighted *italic* in the text.

1. Antiretrovirals as single-ingredient formulations for use in adults and adolescents:

1.1. Nucleoside/Nucleotide Reverse Transcriptase Inhibitors

- Abacavir, tablet 300 mg; 600 mg
- Didanosine, capsule (enteric-coated) 200 mg; 250 mg; 400 mg, tablet (buffered) 100 mg; 150 mg; 200 mg
- Emtricitabine, capsule 200 mg
- Lamivudine, tablet 150 mg; 300 mg
- Stavudine, capsule 30 mg
- Tenofovir disoproxil fumarate, tablet 300 mg
- Zidovudine, tablet 300 mg, capsule 250 mg, solution (i/v) 10 mg/ml

1.2. Non-Nucleoside Reverse Transcriptase Inhibitors

- Efavirenz, capsule 200 mg, tablet 600 mg
- Nevirapine, tablet 200 mg

1.3. Protease Inhibitors

- *Atazanavir, capsule 150 mg; 300 mg*
- Indinavir, capsule 200 mg; 400 mg
- Nelfinavir, tablet 250 mg; 625 mg
- Ritonavir, capsule 100 mg, tablet (heat-stable) 100 mg
- Saquinavir, capsule 200 mg; 500 mg

2. Antiretrovirals as single-ingredient formulations for use in children:

2.1. Solid dosage formulations of

- Abacavir, tablet 60 mg
- Didanosine, capsule (enteric-coated) 125 mg
- Efavirenz, capsule 50 mg; 100 mg
- Lamivudine, tablet 30 mg
- *Nevirapine, tablet 50 mg; 100 mg*
- *Ritonavir, tablet (heat-stable) 25 mg*
- Zidovudine, tablet 60 mg; 100 mg

2.2. Solutions or dissolvable formulations of

- Abacavir, oral liquid 100 mg/5ml
- Emtricitabine, oral liquid 50 mg/5ml
- Lamivudine, oral liquid 50 mg/5ml
- *Nevirapine, oral liquid 50 mg/5ml, sachet/granules 6 mg*
- *Zidovudine, oral liquid 50 mg/5ml, sachet/granules 12 mg*

3. Anti-retrovirals as fixed-dose combinations (FDC) for adults and adolescents:

3.1. Reverse Transcriptase Inhibitors

- Lamivudine + Zidovudine, tablet 150 mg + 300 mg
- Lamivudine + Stavudine + Nevirapine, tablet 150 mg + 30 mg + 200 mg
- Lamivudine + Zidovudine + Nevirapine, tablet 150 mg + 300 mg + 200 mg
- Tenofovir + Emtricitabine, tablet 300 mg + 200 mg
- Tenofovir + Lamivudine, tablet 300 mg + 300 mg
- Tenofovir + Efavirenz + Emtricitabine, tablet 300 mg + 600 mg + 200 mg
- Tenofovir + Efavirenz + Lamivudine, tablet 300 mg + 600 mg + 300 mg

3.2. Protease Inhibitors

- *Atazanavir + Ritonavir, tablet (heat stable) 150 mg + 50 mg; 300 mg + 100 mg*
- Lopinavir + Ritonavir, capsule 133,3 mg + 33,3 mg;
tablet (heat-stable) 200 mg + 50 mg

4. Anti-retrovirals as fixed-dose combinations (FDC) for paediatric use:

4.1. Reverse Transcriptase Inhibitors

- Lamivudine + Abacavir, tablet 30 mg + 60 mg
- Lamivudine + Zidovudine, tablet 30 mg + 60 mg
- *Lamivudine + Stavudine, tablet 30 mg + 6 mg*
- *Lamivudine + Abacavir + Nevirapine, tablet 30 mg + 60 mg + 50 mg*
- *Lamivudine + Stavudine + Nevirapine, tablet 30 mg + 6 mg + 50 mg*
- Lamivudine + Zidovudine + Abacavir, tablet 30 mg + 60 mg + 60 mg
- *Lamivudine + Zidovudine + Nevirapine, tablet 30 mg + 60 mg + 50 mg*

4.2. Protease Inhibitors

- Lopinavir + Ritonavir, tablet (heat-stable) 100 mg + 25 mg

5. Medicines to treat HIV/AIDS related conditions:

5.1. Antibacterial agents:

- Azithromycin
- Benzylpenicillin
- Cefixime
- Ceftriaxone
- Ciprofloxacin
- Clarithromycin
- Clindamycin
- Spectinomycin
- Sulfadiazine
- Sulfamethoxazole + Trimethoprim

5.2. Antiprotozoal, antifungal and antimycobacterial agents:

- Amphotericin B
- Dapsone
- Fluconazole
- Folinic acid
- Itraconazole
- Pentamidine
- Pyrimethamine
- Rifabutin

5.3. Antiviral agents

- Aciclovir
- Ganciclovir

5.4. Anti-cancer drugs

- Bleomycin - Etoposide
- Vinblastine - Vincristine

5.5. Palliative care drugs

- Amitriptyline
- Chlorphenamine
- Codeine
- Ibuprofen
- Loperamide
- Morphine (oral formulation)

Article 3. How to submit an Expression of Interest

In order to submit an expression of interest for product evaluation, the manufacturer must send the requested documentation, arranged according to the information provided on the WHO Prequalification of Medicines Programme web site at www.who.int/prequal/ section "Information for Applicants".

Deadline for submission: December 31, 2009

Article 4. Quality assessment procedure following submission of an expression of interest by a manufacturer

The quality assessment is undertaken to evaluate whether the pharmaceutical product being evaluated meets the requirements recommended by WHO, and is manufactured in compliance with good manufacturing practices (GMP).

The procedure established by WHO for quality assessment incorporates:

- general understanding of the production and quality control activities of the manufacturer;
- assessment of product data and information on safety, efficacy and quality submitted by the manufacturer, including product formulation, manufacture and test data and results;
- assessment of the manufacturing site's adherence to GMP, and its consistency in production and quality control of starting materials, with specific emphasis on active pharmaceutical ingredients, and finished product;
- assessment of clinical testing units or organizations (i.e. parties performing one or more clinical trials with the product) for compliance with good clinical practices and good laboratory practices, as appropriate;
- random sampling and testing of medicines supplied.

Previous evaluation conducted by the relevant National Drug Regulatory Authority (NDRA) may be taken into account during the evaluation conducted by WHO, provided that NDRA has expertise in the product area.

Once WHO is satisfied that quality assessment has been completed for the manufacturer of the relevant starting materials, the finished pharmaceutical product, and the clinical testing units, and that the product meets WHO recommended standards, the product (as produced at the specified manufacturing site) is added to the [WHO List of Prequalified Products](#).

Article 5. References and further information

For further information on the WHO Prequalification of Medicines Programme, please visit the Programme's web-site at: www.who.int/prequal/.

For further information on WHO treatment guidelines, please consult:

1. WHO guidelines on "Antiretroviral therapy for HIV infection in adults and adolescents: recommendations for public health approach", WHO, Geneva 2006; available at: <http://www.who.int/entity/hiv/pub/guidelines/artadultguidelines.pdf>
2. WHO guidelines on "Antiretroviral therapy for HIV infection in infants and children: recommendations for public health approach", WHO, Geneva 2006 available at: <http://www.who.int/hiv/pub/guidelines/paediatric020907.pdf>
3. Report of meetings on paediatric ARV medicines; available at: <http://www.who.int/hiv/events/paediatricmeetingreport.pdf>