

7th Invitation
to manufacturers of antituberculosis medicines
to submit an Expression of Interest (EOI) for product evaluation to the
WHO Prequalification Programme
(June 2007)

To support national and global efforts to increase access to and the affordability of care and treatment of tuberculosis, WHO, together with UNICEF, UNAIDS and UNITAID, invites manufacturers of selected pharmaceutical products to submit **Expressions of Interest (EOIs)** for product evaluation. (The first Invitation for EOI for antituberculosis medicines was published in 2002 and the 6th EOI was published in May 2005.)

Article 1. Procedure for this EOI

The current Invitation for EOI 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, published as part of the 37th report of the Committee (no. 908 of the WHO Technical Report Series) in 2003, 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 for EOI includes 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 7th Invitation

The ultimate aim of this 7th EOI is to increase the range of selected products and sources available in relation to treatment for tuberculosis. The medicines listed in the 7th EOI have been identified by WHO Department of tuberculosis as vital to effective treatment for people living with tuberculosis. These products are included either in the [WHO Model List of Essential Medicines](#) and/or in the [Treatment of tuberculosis: guidelines for national programmes](#), and [Guidelines for the programmatic management of drug-resistant tuberculosis](#).

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.

1. Single ingredient first-line antituberculosis medicines

- Ethambutol, tablet 400 mg
- Isoniazid, tablet 300 mg
- Pyrazinamide, tablet 400 mg
- Rifampicin, capsule 150 mg; 300 mg
- Streptomycin, powder for injection 1g (vial)

2. Fixed dose combination products of first-line antituberculosis medicines

- Isoniazid + Rifampicin, tablet 75 mg + 150 mg; tablet 150 mg + 150 mg
- Ethambutol + Isoniazid, tablet 400 mg + 150 mg
- Ethambutol + Isoniazid + Rifampicin, tablet 275 mg + 75 mg + 150 mg
- Ethambutol + Isoniazid + Pyrazinamide + Rifampicin, tablet 275 mg + 75 mg + 400 mg + 150 mg

3. Single ingredient second-line antituberculosis medicines

- Amikacin, 250 mg/ml (vial 2 ml, 4 ml); powder for injection 1g (vial)
- Capreomycin, powder for injection 1g (vial)
- Cycloserine, capsule 250 mg
- Ethionamide, coated tablet 125 mg; 250 mg
- Kanamycin, powder for injection 1g (vial)
- Levofloxacin, tablet 250 mg
- Moxifloxacin, tablet 400 mg
- Ofloxacin, tablet 200 mg; 400 mg
- Prothionamide, coated tablet 250 mg
- P-aminosalicylic acid, granules 4g
- P-aminosalicylic sodium, granules 100 g

4. Scored solid dosage formulations for children*, preferably dispersible

- Ethambutol, tablet 100 mg
- Isoniazid, tablet 50 mg; 100 mg
- Pyrazinamide, tablet 150 mg

** Please note that paediatric formulations are currently under review and new recommendations on desirable strengths and combinations are due by April 2009.*

Article 3. How to submit an EOI

In order to submit an expression of interest for product evaluation, the manufacturer must send the required 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: 1 April 2009

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

The quality assessment is undertaken to assess 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 the NDRA has expertise in the product area. If appropriate, the relevant NDRA may be invited to collaborate with WHO on the quality assessment. Any manufacturer who submits a product for evaluation, is therefore encouraged to authorize its NDRA to discuss relevant product files with WHO representatives, during assessments and inspections, if required (subject to appropriate confidentiality provisions, if necessary).

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 Medicines](#).

Article 5. References and further information

For further information on the WHO Prequalification Programme, please visit the Programme's web-site at: www.who.int/prequal. Should you have any questions relating to the procedure for responding to an EOI, please write to the WHO Prequalification Programme at its email address: prequal@who.int. Your question(s) will be directed to the prequalification team member who can best advise you.

For further information on WHO treatment guidelines, please consult:

1. "Treatment of tuberculosis: guidelines for national programmes", 3rd edition, WHO, Geneva 2003; available at:
http://whqlibdoc.who.int/hq/2003/WHO_CDS_TB_2003.313_eng.pdf
2. And its Chapter 4 "Standardized treatment regimens", revised in June 2004; available at:
http://www.who.int/tb/publications/tb_2003_313_chap4_rev.pdf
3. "Guidelines for the programmatic management of drug-resistant tuberculosis", WHO, Geneva 2006; available at:
http://whqlibdoc.who.int/publications/2006/9241546956_eng.pdf