

10th Invitation
to manufacturers of antituberculosis medicines
to submit an Expression of Interest (EOI) for product evaluation to the
WHO Prequalification Programme
(August 2010 - amended February 2011)

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.

Article 1. Procedure for this EOI

The current Invitation is published in accordance with the *Procedure for prequalification of pharmaceutical products*, adopted in 2001 by the 37th WHO Expert Committee on Specifications for Pharmaceutical Preparations, and amended subsequently as part of the 43rd report of the Committee, published as [No. 953 of the WHO Technical Report Series](#) in 2009.

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 in the 10th Invitation

The ultimate aim of this 10th EOI is to increase the range of selected products and sources available in relation to treatment for tuberculosis. The recommended active ingredients, dosage forms and strengths listed in this document have been identified by WHO's Stop TB Department for effective treatment of people suffering from tuberculosis. These formulations are included either in the WHO Model List of Essential Medicines¹ and/or in the WHO standard treatment guidelines²

¹ WHO Model List of Essential Medicines. 16th list, March 2009

http://www.who.int/selection_medicines/committees/expert/17/sixteenth_adult_list_en.pdf

WHO Model List of Essential Medicines. For Children. Second list, March 2009

http://www.who.int/selection_medicines/committees/expert/17/second_children_list_en.pdf

² WHO. Treatment of tuberculosis: guidelines for national programmes. 3rd edition. WHO/CDS/TB/2003.313.

http://www.who.int/tb/publications/cds_tb_2003_313/en/

WHO. Guidelines for the programmatic management of drug-resistant tuberculosis. Emergency update 2008. WHO/HTM/TB/2008.402

http://www.who.int/tb/publications/2008/programmatic_guidelines_for_mdrtb/en/index.html

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 anti-tuberculosis medicines

- Ethambutol (E), film coated tablet/capsule 200mg; 275mg
- Ethambutol, coated tablet/ capsule 400 mg
- Isoniazid, tablet /capsule 300 mg
- Pyrazinamide (Z), film coated tablet/capsule 250mg
- Pyrazinamide, tablet /capsule 400 mg; 500 mg
- Rifampicin, capsule 150 mg; 300 mg
- Streptomycin, powder for injection 1g (vial) *
- Streptomycin, powder for injection 0.75 g (vial) *

2. Fixed dose combination products of first-line anti-tuberculosis medicines

- Isoniazid + Rifampicin,
 - coated tablet / capsule 75 mg + 150 mg;
 - coated tablet / capsule 150 mg + 150 mg
 - coated tablet / capsule 150 + 300 mg
- Ethambutol + Isoniazid,
 - coated tablet /capsule 400 mg + 150 mg
- Ethambutol + Isoniazid + Rifampicin,
 - coated tablet/capsule 275 mg + 75 mg + 150 mg
- Isoniazid + Pyrazinamide + Rifampicin,
 - coated tablet/capsule 150mg + 500mg + 150mg
- Ethambutol + Isoniazid + Pyrazinamide + Rifampicin,
 - coated tablet 275 mg + 75 mg + 400 mg + 150 mg
- Isoniazid + Pyrazinamide+ Rifampicin,
 - film coated tablet/capsule 75mg + 400mg + 150mg

3. Single ingredient second-line anti-tuberculosis medicines

- Amikacin, solution injection 500 mg/2 ml vial, amp; powder for injection 1g vial, amp *
- Capreomycin, powder for injection 1g, vial *
- Cycloserine, capsule 250 mg
- Ethionamide, tablet /capsule 250 mg
- Kanamycin, powder for injection 1g, vial *
- Kanamycin, powder for injection 500 mg, vial *
- Levofloxacin, tablet /capsule 250 mg, tablet 500 mg, tablet 750 mg
- Moxifloxacin, tablet /capsule 400 mg
- Ofloxacin, tablet /capsule 200 mg; 400 mg
- Prothionamide, tablet /capsule 250 mg
- Para-Aminosalicylic Acid (PAS) sachets, 4 g granules
- PAS Sodium 100 g jar granules, 4g / 9.2 g sachets granules; powder for oral solution sachets
- Terizidone, tablet/capsule, 250 mg; 300 mg

4. Scored solid dosage formulations for children, preferably dispersible

- Ethambutol, coated tablet 100 mg
- Isoniazid, coated tablet 50 mg; 100 mg, 150 mg
- Pyrazinamide, coated tablet 150 mg
- Ethambutol oral liquid 25mg/ml.
- Pyrazinamide oral syrup 30mg/ml.

* with or without diluent water for injection 5 ml vial

***Note:** The fixed dose combination products of formulation for children suggested in March 2009 by the Expert Committee are subject to the final conclusions of the feasibility study being carried out.*

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".

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