

**8th Invitation to
manufacturers of antimalarial medicines
to submit an Expression of Interest (EOI) for product evaluation to the
WHO Prequalification of Medicines Programme**
(August 2009)

To support national and global efforts to increase access to and the affordability of care and treatment of malaria, 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 antimalarial medicines was published in 2002.

Article 1. Procedure for this Invitation to 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 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 malaria. The medicines listed in the 8th Invitation have been identified by WHO Global Malaria Programme as vital to effective treatment for people living with malaria. These products are included either in the [WHO Model List of Essential Medicines](#) and/or in the [WHO guidelines for the treatment of malaria](#).

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. The appropriate solid dosage formulations, which are scored for flexible dosing purposes, should be supported by relevant evidence on equal distribution of active ingredients in the scored products, especially in case of fixed-dose combination products.

1. Artemisinin-based fixed dose oral combination formulations

- Artemether + Lumefantrine,
tablet 20 mg + 120 mg;
tablet 40 mg + 240 mg;
tablet 60 mg + 360 mg;
tablet 80 mg + 480 mg

- Artesunate + Amodiaquine,
tablet 25 mg + 67.5 mg;
tablet 50 mg + 135 mg;
tablet 100 mg + 270 mg

- Artesunate + Amodiaquine,
tablet 25 mg + 76.5 mg;
tablet 50 mg + 153 mg;
tablet 100 mg + 306 mg

- Dihydroartemisinin + Piperaquine Phosphate,
tablet 40 mg + 320 mg;
tablet 20 mg + 160 mg;

2. Artemisinin-based fixed dose combination or co-blistered oral formulations

- Artesunate + Mefloquine,
tablet 25 mg + 125 mg;
tablet 50 mg + 250 mg;
tablet 100 mg + 250 mg

- Artesunate + Sulfadoxine + Pyrimethamine,
tablet 25 mg + 250 mg + 12.5 mg
tablet 50 mg + 500 mg + 25 mg;
tablet 100 mg + 500 mg + 25 mg

3. Artemisinin-based fixed dose combination or co-blistered oral paediatric formulations, preferably dispersible

- Artemether + Lumefantrine
- Artesunate + Amodiaquine
- Artesunate + Mefloquine
- Artesunate + Sulfadoxine + Pyrimethamine

4. Artemisinin-based single-ingredient formulations

- Artemether, oily injection 20 mg/ml; 40 mg/ml; 80 mg/ml
- Artesunate, powder for injection 60 mg (vial)
- Artesunate, suppositories 50 mg; 100 mg; 200 mg; 400 mg
- Artesunate, tablet* 25 mg; 50 mg; 100 mg

5. Other antimalarial medicines

- Mefloquine, tablet 250 mg
- Sulfadoxine + Pyrimethamine, tablet 500 mg + 25 mg

Product presentations which support adherence to treatment and rational drug use are strongly encouraged.

* Artesunate tablets to be used only in combination with either Mefloquine or Sulphadoxine + Pyrimethamine

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 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 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 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 Products](#).

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: "WHO guidelines for the treatment of malaria", WHO, Geneva 2006; available at: <http://www.who.int/malaria/docs/TreatmentGuidelines2006.pdf>