



**A NEW
PERSPECTIVE
ON TB DRUG
PROCUREMENT.**

Invitation for Expressions of Interest To Manufacturers of First-Line Anti-Tuberculosis Pharmaceuticals

The Global Drug Facility (GDF) intends to issue, via its procurement agent, (GTZ, German Organization for Technical Cooperation), an Invitation to Bid (ITB) in a tender for the supply of first-line anti-TB drugs to countries eligible to receive GDF support. The ITB is expected to be issued in October/November 2006. The products included in the ITB will include:

- **Ethambutol 400mg (E400)** film coated tablets: Blister Pack and Loose tablets in HDPE container
- **Ethambutol 100mg (E100)** film coated tablets and dispersible: Blister Pack, Loose tablets in HDPE container, sachets
- **Isoniazid 300mg (H300)** tablets: Blister Pack and Loose tablets in HDPE container
- **Isoniazid 100mg (H100) & 50mg (H50)** tablets and dispersible: Blister Pack, Loose tablets in HDPE container, sachets
- **Pyrazinamide 400mg (Z400)** tablets: Blister Pack and Loose tablets in HDPE container
- **Pyrazinamide 150mg (Z150)** tablets and dispersible: Blister Pack, Loose tablets in HDPE container, sachets
- **RHZE150/75/400/275 (4-FDC)** film coated tablets: Blister Pack and Loose tablets in HDPE container
- **RHE150/75/275 (3-FDC)** film coated tablets: Blister Pack and Loose tablets in HDPE container
- **RHZ 60/30/150 (3FDC)** tablets and dispersible: Blister Pack, Loose tablets in HDPE container, sachets
- **RH150/75 (2-FDC)** film coated tablets: Blister Pack and Loose tablets in HDPE container
- **RH150/150 (2-FDC)** film coated tablets: Blister Pack and Loose tablets in HDPE container
- **RH60/60 (2-FDC)** tablets and dispersible: Blister Pack, Loose tablets in HDPE container, sachets **RH60/30 (2-FDC)** tablets and dispersible: Blister Pack, Loose tablets in HDPE container, sachets
- **EH400/150 (2-FDC)** film coated tablets: Blister Pack and Loose tablets in HDPE container
- **Streptomycin 1g** vials
- **Water for Injection (Solvent)** 5ml vials

Products eligible to be submitted into this tender will need to meet the following criteria:

1. Will be manufactured at a site that has been inspected by WHO as a part of the WHO Procurement, Quality and Sourcing Project: Access to Tuberculosis Drugs of acceptable quality (<http://mednet3.who.int/prequal/>) and found operating at an acceptable level of compliance with WHO Good Manufacturing Practices (GMP) or in a manufacturing site located in a



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highly regulated country such as an ICH¹ country or equivalent, and inspected by a stringent official inspectorate for compliance with GMP (in terms of the legislation of the relevant country).

2. Have been prequalified by WHO under the WHO Procurement, Quality and Sourcing Project: Access to Tuberculosis Drugs of acceptable quality; or
3. Be found acceptable to the GDF through an *ad hoc assessment process** which assesses products based on the information provided in the attached Pharmaceutical Product Questionnaire.

*Please note:

- I. Products that have already gained WHO prequalification need not be submitted into this ad hoc assessment process.
- II. Products that have a valid marketing authorization or license for export in a highly regulated country such as an ICH country or equivalent and have not gained WHO prequalification need to be submitted into this ad hoc assessment process i.e. a Pharmaceutical Product Questionnaire must be completed.
- III. Paediatric Products already submitted into the *ad hoc assessment process for paediatric anti-TB drugs* conducted from November 2005 should be listed, but the Pharmaceutical Product Questionnaire need not be repeated. However, any additional/new data developed for a particular product for which an original submission was made in November 2005, should be provided as per the Pharmaceutical Product Questionnaire requirements.

All submissions will be assessed for acceptability to the GDF and the suppliers will be notified in advance of the tender which products it is able to offer in the next GDF tender.

All manufacturers interested in participating in the next GDF tender are requested to submit, via registered courier, the Pharmaceutical Product Questionnaire and all the documents and samples requested (where applicable) for each product under consideration to the following address, no later than **22 September 2006**. Data should be submitted in hard copy AND as electronic data files (e.g. on writable CD-ROM).

Subject: Global Drug Facility Tender, 2006
Attention: Sarah Schmitt
Procurement Team leader, Global Drug Facility
Stop TB Department
World Health Organization
20 Avenue Appia
1211 Geneva 27
Switzerland
Tel: +41-22-791-3971/Fax: +41-22-791-4886
Email: schmittsa@who.int

¹ International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use: www.ich.org

ANNEX 1 : PHARMACEUTICAL PRODUCT QUESTIONNAIRE

Please Note: Adjudication criteria are mentioned under each question, (where applicable), *in Italics*.

I Product identification

Product Number of this tender:.....

Active Pharmaceutical Ingredient(s) (use INN where it exists):
.....

Generic name of the product:
.....

Dosage form : Tablets Capsules Ampoules Vial Other:
Strength per dosage unit:
.....

Route of administration : Oral Intramuscular
 Intravenous Subcutaneous
 Other:

Pack size: 50 100 1000 1000ml Other

List the standard batch size:

II. Manufacturer of the product

Name, address and activities of the manufacturer (or contract manufacturer):

Name	Physical address	Telephone number, Facsimile number and e-mail contact details

II.1 The site listed above is licensed by the relevant Regulatory Authority to perform the activity?

Yes No

Answer "No" may lead to disqualification of the product for the LICB.

II.2 Is the manufacturing site pre-qualified by WHO for GMP compliance under the TB Prequalification Project?

Yes No

Answer "No" may lead to disqualification of the product for the LICB

Please attach a copy WHO notification of GMP Compliance under the TB prequalification Project

II.3 Is the manufacturing site certified for GMP compliance by a stringent Regulatory Authority party to the Pharmaceutical Inspection Cooperation Scheme or International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use?

Yes No

Answer "No" may lead to disqualification of the product for the LICB

Please attach a copy of the notification of GMP Compliance by the stringent Regulatory Authority

III. Supplier identification

(to be filled in if not identical to that indicated in question II)

Name.....

Address:
.....
.....

Telephone number:.....
Facsimile number:.....
E-mail:.....

III.1 Please submit a "Letter of Authority" issued by the manufacturer uniquely for the intended LICB.

Absence of the letter may lead to disqualification of the product for the LICB.

Link with the product:

- Marketing license holder
- Distributor
- Manufacturer
- Other (Please indicate)

IV. Regulatory situation (licensing status) in the country of manufacture

Product registered and currently marketed license
n°.....
Please attach a copy

Product registered for export only license
n°.....
Please attach a copy

IV.1 Product has to be either registered for use in the country of manufacture or has to be registered for export to qualify.

IV.2 Please attach a Certificate of Pharmaceutical Product according to the WHO Certification Scheme to qualify (WHO Technical Report Series No. 863. Earlier version is not acceptable).

V. Regulatory situation (licensing status) in other countries

List other countries (and licensing numbers) where the product is registered (*per product*) and is currently marketed:

.....

VI. Finished product specifications

- BP Edition (year)
 USP Edition (number and year)
 International Pharmacopoeia. Edition (Volume and year)
 Other

VI.1 Please attach a copy of the finished product specification, if different from BP, USP or International Pharmacopoeia specification.

Absence of copy may lead to disqualification of the product for the LICB

VI.2 Attach a copy of the certificate of analysis for a sample batch.

Absence of copy may lead to disqualification of the product for the LICB

Are you willing to provide necessary information (analytical method) for the tests to be replicated by another control laboratory?

Yes No

"No" may lead to disqualification of the product for the LICB

VII. Stability

VII.1 Stability testing data available:

Yes No

Answer **"No"** may lead to disqualification of the product for the LICB

If yes, type and conditions of testing:

Accelerated testing 40±2°C/ 75 ±5 % RH/ 6 months other (please specify)

VII.2 In the same packaging as specified under point I (page 1)

Yes No

Answer **"No"** may lead to disqualification of the product for the LICB

VII.3

- real time testing
 30±2°C/ 65 ±5 % RH and with test results at every 3 months in the first year, every 6th month in the second year, and then annually
 Other (please specify)

VII.4 In the same packaging as specified under point I (page 1)

Yes No

Answer “No” may lead to disqualification of the product for the LICB.

VII.5 Attach stability report(s)

Absence of stability report(s) may lead to disqualification of the product for the LICB

VIII. Label and insert information

VIII.1 Shelf-life: 5 years 4 years 3 years 2 years Not determined

Answer “**Not determined**” may lead to disqualification of the product for the LICB

IX. Samples

IX.1 Free non-returnable samples to be submitted with bids at time of LICB

Yes No

Answer “No” may lead to disqualification of the product for the LICB

X. Therapeutic equivalence

X.1 For Rifampicin containing FDC tablets a bio-equivalence study report for at least the Rifampicin component should be submitted, in compliance with WHO Guidelines and Good Clinical Practices. (WHO Technical Report series, No.863)

Absence of a bio-equivalence study report submitted may lead to disqualification of the product for the LICB

For other products the therapeutic equivalence is demonstrated:

By in vivo bio-equivalence studies

- Reference product:
- Number of volunteers:
- Country of study:
- Performed (year):

Or by another method claimed by the supplier/manufacturer

(Please describe briefly):

Or by comparative in vitro dissolution tests

- Reference product:
- not demonstrated not relevant unknown

Attach copy of the study report, unless not relevant

XI. Active Pharmaceutical Ingredients(s) (APIs)

(In case more than one active ingredient is used, answer this question for each API)

Manufacturer (name, physical address + country):

.....

XI.1 GMP certified by:

Yes (attach a copy of the GMP certificate if any) **No** **Unknown**

Answer "No or Unknown" may lead to disqualification of the product for the LICB

XI. 2 Specifications and standard test methods exist for each API and excipient

Yes **No**

Answer "No" may lead to disqualification of the product for the LICB

XI.3 Limits in % for the assay in active ingredient(s):

95-105% **90-110 %**

Each API used (in INN if any):

.....

XI.4 Has a Certificate of suitability to the European Pharmacopoeia (CEP) been issued?

Certificate N°:

The CEP is in our possession (including annex if any)

If it is, attach a copy

XI.5 A Drug Master File (DMF) has been submitted to (specify country (ies):.....

The full or open part of the DMF is in our possession

Quality standard:

XI.6 BP USP EP International Pharmacopoeia

Other (e.g. "in-house")

Please attach a copy of the API specification, if different from BP, USP or International Pharmacopoeia specification.

Absence of copy may lead to disqualification of the product for the LICB

No Pharmacopoeia monograph exists*

***If there is no monograph in a recognized Pharmacopoeia, then the following information should be provided:**

XII. Chemical structure:

- If relevant, the isomeric nature of the active ingredient, including stereochemical configuration (e.g. acetate, pure (S)-isomer, 50/50 mixture of (Z)- and (E)-isomers;
- The solubility of the active ingredient in water at 25 or 35C
- The solubility of the active ingredient in other solvents such as ether, ethanol, acetone, and buffers if different pH (if the active ingredient is acidic or basic),
- Other relevant physicochemical characteristics of the active ingredient such as partition coefficient (usually octanol/water) and the existence of polymorphs;
- Copies of infrared, nuclear magnetic resonance (proton and C-13), ultraviolet and mass spectra;
- Information on the chemical stability of the API, and on physicochemical stability if relevant (e.g. formation of a hydrate, change of polymorphic form).

XIII. Commitment

I, the undersigned,
.....(position in the company, e.g. General Manager, Authorised Person, Responsible Pharmacist), acting as responsible person for the company.....(name of the company), certify that the information provided (above) is correct and true (if the product is marketed in the country of origin, tick the adequate following box) and I certify that the product offered is identical in all aspects of manufacturing and quality to that marketed in (country of origin), including formulation, method and site of manufacture, sources of active and excipient starting materials, quality control of the product and starting material, packaging, shelf-life and product information.

and I certify that the product offered is identical to that marketed in (name of country),
except:
.....
(e.g. formulation, method and site of manufacture, sources of active and excipient starting materials, quality control of the finished product and starting material, packaging, shelf-life, indications, product information)

Date:.....

Signature.....