



# West African Health Organization

Promoting better health through Regional Integration

MPDER-MRH/EOI/19/007-00

## WEST AFRICA MEDICINES REGULATION HARMONIZATION INITIATIVE

### CALL FOR EXPRESSION OF INTEREST (EOI) FOR REGIONAL JOINT MEDICAL PRODUCTS EVALUATION FOR HIV INFECTIONS AND RELATED DISEASES

#### INTRODUCTION

The West Africa Medicines Regulation Harmonization (WA-MRH) Project has agreed a single process for regional medical product evaluation to enable the registration of medicinal products in the 15 ECOWAS Member States.

This call is an invitation to manufacturers of anti-malaria medicines to submit Expressions of Interest (EOI) for the Regional Joint Medical Products evaluation for registration under this project.

The invitation is published in accordance with the document titled “*WA-MRH Regional Joint Medical Product Evaluation Procedure for pharmaceutical product dossier*”, which is dated July 2019 and is available on WAHO Website ([www.wahooas.org](http://www.wahooas.org)) under the section **Resources**, sub-section **Publications and Research**, sub sub-section **Essential Medicines and Vaccines**” and also under the section **Procurement**.

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)
- Product samples, which must adhere to the requisite specifications.

If an evaluation demonstrates that the above three criteria meet the harmonized ECOWAS Common Technical Document (CTD) standards, it would be eligible for inclusion in the products register of each NMRA in all 15 ECOWAS Member States. Such an inclusion would be effected in a Member State on payment of the applicable registration fee by the Manufacturer to the NMRA of that Member State, but this eligibility for inclusion will lapse after two (2) years from the date of issuance of regional recommendation.



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## MEDICINAL PRODUCTS FOR THIS EOI

The aim of this EOI is to evaluate a specific range of medical products available in relation to the management of HIV Infections and Related Diseases. The medicines listed in this invitation have been identified by the Expert Working Group for Medical Product Dossier Evaluation and Registration of the WA-MRH Project as vital to effective treatment of HIV Infections and Related Diseases, based on WAHO's assessment of the priority health needs in the region, and WHO's evidenced-based treatment guidelines.

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

- **Nucleoside/Nucleotide Reverse Transcriptase Inhibitors:**
  - Lamivudine, tablet, 300mg
- **Non-Nucleoside Reverse Transcriptase Inhibitors:**
  - Efavirenz, tablet 400mg
  - Etravirine, tablet, 200mg
- **Integrase Inhibitors:**
  - Dolutegravir, tablet 50mg, preferably scored and dispersible
  - Raltegravir, tablet 400mg

### Antiretrovirals as single-ingredient formulations for use in children:

- **Solid oral dosage formulations of:**
  - Dolutegravir, tablet 10mg scored and dispersible or 5 mg dispersible
  - Raltegravir, dispersible tablet 5mg (scored) and 50mg (scored)
- **Oral liquid or powder for oral liquid:**
  - Lamivudine, 50mg/5ml
  - Nevirapine, 50mg/5ml
  - Zidovudine, 50mg/5ml

### Antiretrovirals as fixed-dose combinations (FDC) for adults and adolescents:

- **Nucleoside/Nucleotide Reverse Transcriptase Inhibitors:**
  - Lamivudine/Abacavir, tablet (preferably scored) 300mg/600mg



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- **Nucleoside/Nucleotide Reverse Transcriptase Inhibitors plus Non-nucleoside Reverse Transcriptase Inhibitors:**
  - Emtricitabine/Tenofovir disoproxil fumarate/Efavirenz, tablet 200mg/300mg/400mg
  - Lamivudine/Tenofovir disoproxil fumarate/Efavirenz, tablet 300mg/300mg/400mg
  - Lamivudine/Tenofovir disoproxil fumarate/Efavirenz, tablet 300mg/300mg/600mg
- **Protease Inhibitors:**
  - Atazanavir/Ritonavir, tablet (heat stable) 300mg/100mg
  - Darunavir/Ritonavir, tablet (heat stable) 800/100mg, 600/100mg, 300mg/50mg, 400mg/50mg
- **Nucleotide Reverse Transcriptase Inhibitors plus Non-nucleoside Reverse Transcriptase Inhibitors plus Integrase Inhibitors:**
  - Emtricitabine/Tenofovir disoproxil fumarate/Dolutegravir, tablet 200mg/300mg/50mg
  - Lamivudine/Tenofovir disoproxil fumarate/Dolutegravir, tablet 300mg/300mg/50mg

### Antiretrovirals as fixed-dose combinations (FDC) for paediatric use:

- **Nucleoside/Nucleotide Reverse Transcriptase Inhibitors:**
  - Lamivudine/Abacavir, tablet 30 mg/60 mg scored and dispersible
  - Lamivudine/Abacavir, tablet 60 mg/120 mg scored and dispersible
  - Lamivudine/Zidovudine, tablet 30 mg/60 mg scored and dispersible
- **Nucleoside/Nucleotide Reverse Transcriptase Inhibitors plus Non-nucleoside Reverse Transcriptase Inhibitors:**
  - Lamivudine/Abacavir/Efavirenz, tablet 75 mg/150 mg/150 mg scored and dispersible
- **Nucleoside/Nucleotide Reverse Transcriptase Inhibitors plus Protease Inhibitors:**
  - Lamivudine/Abacavir, granules/minitablets/pellets 15 mg/30 mg co-mixed with Lopinavir/Ritonavir, granules/minitablets/pellets (heat stable) 40 mg/10 mg
  - Lamivudine/Zidovudine, granules/minitablets/pellets 15 mg /30 mg co-mixed with Lopinavir/Ritonavir, granules/minitablets/pellets (heat stable) 40mg/10mg



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- **Protease Inhibitors:**
  - Darunavir/Ritonavir, tablet (heat-stable), 120 mg/20 mg
  - Lopinavir/Ritonavir, tablet (heat-stable) 100 mg/25 mg,
  - Lopinavir/Ritonavir, granules/minitablets/pellets (heat stable) 40 mg/10 mg
  - Lopinavir/Ritonavir, oral solution 80/20 mg/ml
- **Nucleoside/Nucleotide Reverse Transcriptase Inhibitors plus Integrase Inhibitors:**
  - Lamivudine/Abacavir/Dolutegravir, tablet 30 mg/60 mg/5 mg dispersible

### COMPLEMENTARY LIST OF NON-PRIORITY ARV PRODUCTS

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

- **Nucleoside/Nucleotide Reverse Transcriptase Inhibitors:**
  - Abacavir, tablet 300 mg, 600 mg
  - Lamivudine, tablet 150 mg
  - Tenofovir disoproxil fumarate, tablet 300 mg
  - Zidovudine, tablet 300 mg; capsules 250 mg
- **Non-Nucleoside Reverse Transcriptase Inhibitors:**
  - Efavirenz, tablet 600 mg
  - Nevirapine, tablet 200 mg
  - Etravirine, tablet 100 mg
- **Protease Inhibitors:**
  - Atazanavir, capsule 150 mg; 300 mg
  - Darunavir, tablet 400mg; 600mg; 800 mg
  - Ritonavir, tablet (heat-stable) 100 mg

#### Antiretrovirals as single-ingredient formulations for use in children:

- **Solid dosage formulations of:**
  - Efavirenz, tablet (scored) 100 mg and preferably dispersible
  - Etravirine, tablet 25 mg, and preferably dispersible
  - Lamivudine, tablet (scored) 30 mg, and preferably as dispersible
  - Nevirapine, tablet (scored) 20 mg; 100 mg and preferably as dispersible
  - Tenofovir disoproxil fumarate, tablets 150 mg; 200 mg; preferably dispersible
  - Zidovudine, tablet (scored) 60 mg, and preferably as dispersible



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- **Oral solutions or dissolvable formulations of:**
  - Abacavir, 100 mg/5 ml
  - Tenofovir disoproxil fumarate, oral powder 40 mg/measure

### Antiretrovirals as fixed-dose combinations (FDC) for adults and adolescents:

- **Nucleoside/Nucleotide Reverse Transcriptase Inhibitors:**
  - Emtricitabine/Tenofovir disoproxil fumarate, tablet 200 mg/300 mg
  - Lamivudine/Tenofovir disoproxil fumarate, tablet 300 mg/300 mg
  - Lamivudine/Zidovudine, tablet 150 mg/300 mg; tablet 150 mg/250 mg
- **Nucleoside/Nucleotide Reverse Transcriptase Inhibitors plus Non-nucleoside Reverse Transcriptase Inhibitors:**
  - Emtricitabine/Tenofovir disoproxil fumarate/Efavirenz/, tablet 200 mg/300 mg/600 mg
  - Lamivudine/Zidovudine/Nevirapine, tablet 150 mg/300 mg/200 mg; tablet 150 mg/250 mg/200 mg
- **Protease Inhibitors:**
  - Atazanavir/Ritonavir, tablet (heat stable) 150 mg/50 mg
  - Lopinavir/Ritonavir, tablet (heat-stable) 200 mg/50 mg

### Antiretrovirals as co-packaged formulations for adults and adolescents:

- **Nucleoside/Nucleotide Reverse Transcriptase Inhibitors plus Non-nucleoside Reverse Transcriptase Inhibitors**
  - One FDC tablet of Lamivudine/Tenofovir disoproxil fumarate/, 300 mg/300 mg, co-packaged with two single tablets of Nevirapine 200 mg
  - One FDC tablet of Emtricitabine/Tenofovir disoproxil fumarate, 200 mg/300 mg, co-packaged with two single tablets of Nevirapine 200 mg
- **Nucleoside/Nucleotide Reverse Transcriptase Inhibitors plus Protease Inhibitors:**
  - One FDC tablet of Lamivudine/Tenofovir disoproxil fumarate/, 300 mg/300 mg, co-packaged with one FDC tablet (heat stable) of Atazanavir/Ritonavir 300 mg/100 mg
  - One FDC tablet of Emtricitabine/Tenofovir disoproxil fumarate, 200 mg/300 mg, co-packaged with one FDC tablet (heat stable) of Atazanavir/ Ritonavir 300 mg/100 mg
  - One FDC tablet of Lamivudine/Tenofovir disoproxil fumarate, 300 mg/300 mg, co-packaged with one single tablet of Atazanavir 300 mg and one single tablet (heat stable) of Ritonavir 100 mg



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- One FDC tablet of Emtricitabine/Tenofovir disoproxil fumarate, 200 mg/300 mg, co-packaged with one single tablet of Atazanavir 300 mg and one single tablet (heat stable) of Ritonavir 100 mg

### MEDICINES TO TREAT HEPATITIS B OR C IN ADULTS AND ADOLESCENTS

#### Antivirals as single-ingredient formulations for use in adults and adolescents:

- **Hepatitis C**
  - Daclatasvir tablet, 30mg, 60mg (preferably scored)
  - Dasabuvir, tablet 250mg
  - Ledipasvir tablet, 90mg
  - Ribavirin capsule, 200mg, 400mg, 600mg
  - Sofosbuvir tablet, 400mg
  - Velpatasvir tablet, 100mg
- **Hepatitis B**
  - Entecavir tablet, 0.5mg, 1mg scored
  - Tenofovir, tablet 300mg
  - Tenofovir, tablet 150mg, 200mg, preferably dispersible.

#### Antivirals as fixed-dose combinations (FDC) for adults and adolescents:

- **Hepatitis C**
  - Ombitasvir/Paritaprevir/Ritonavir, tablet 12.5mg/75mg/50mg
  - Ombitasvir/Paritaprevir/Ritonavir, tablet 25mg/150mg/100mg
  - Sofosbuvir/ Ledipasvir, tablet 400mg/90mg
  - Sofosbuvir/ Daclatasvir, tablet 400mg/60mg
  - Sofosbuvir/ Daclatasvir, tablet 400mg/30mg
  - Sofosbuvir/Velpatasvir tablet 400mg/100mg

#### Antivirals as single-ingredient formulations for use in children: Paediatric formulations

- **Hepatitis C:**
  - Ribavirin, syrup, 40mg/ml (oral)
- **Hepatitis B**
  - Entecavir, oral solution, 0.05mg/ml



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## HOW TO SUBMIT AN EOI

The Lead Coordinating NMRA for this invitation for EOI is the NMRA of Ghana, the Food and Drug Authority (<http://www.fda Ghana.gov.gh>).

In order to submit an expression of interest for product evaluation, the applicant must do the following:

1. The applicant will pay the management fees of US\$ 500 for the lead coordinating NMRA (FDA-Ghana) for reception, screening, file management and communication when submitting the file. The Bank account details are as follows:

**Food and Drugs Authority**

**Bank of Ghana**

**Account No: 1018631529507**

**Swift Code: BAGHGHAC.**

2. The applicant should download and complete the Market Authorization application (MA) file in accordance with the harmonized Common Technical Document (CTD) format on WAHO Website ([www.wahooas.org](http://www.wahooas.org)) under the section **Resources**, sub-section **Publications and Research**, sub sub-section **Essential Medicines and Vaccines** and also under the section **Procurement**. The completed application MA file should be submitted electronically to the lead coordinating NMRA ([fda@fdaghana.gov.gh](mailto:fda@fdaghana.gov.gh)) with a hard copy sent to Room 316, FDA Head Office, 17 Indian Ocean Street, off Nelson Mandela Avenue, South Legon Commercial Area, Shishie, Accra, GHANA (telephone: +233554456478).
3. The applicant should provide samples of the medical product and reference substances. The sample size shall be in line with the quantity defined by the EWG for Quality Control and published under the **Essential Medicines and Vaccines** section and also under the section **Procurement** on the WAHO website. The samples should be submitted together with the Dossiers to the lead coordinating NMRA (FDA-Ghana).
4. After screening, a certificate of eligibility or non-eligibility for full evaluation will be sent to the applicant by the lead coordinating NMRA. On receipt of a certificate of eligibility the applicant should pay the full evaluation fee within 30 calendar days to the WA-MRH secretariat bank account specified in the certificate:-the applicable fee for the processing of the application.

### a) Certificate of Eligibility

- Applicants in the West Africa Region will pay US\$ 8,000
- Applicants in other regions of Africa will pay US\$ 10,000
- Applicants outside Africa will pay US\$ 12,000





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The full fees for a product evaluation is US\$ 23,750 but WAHO, as the WA-MRH Secretariat, has undertaken to absorb the difference in cost in the initial stages of this project. The full fees may therefore be implemented in future EOIs at a later date.

### b) Certificate of Non-Eligibility

In the event of an applicant receiving a certificate of non-eligibility, the applicant may resubmit another Market Authorization (MA) application file for screening and pay the management fee of US\$ 500 to the lead coordinating NMRA upon resubmission.

## QUALITY CONTROL ASSESSMENT AFTER SUBMISSION OF AN EOI BY AN APPLICANT

As part of the full evaluation for Market Authorization, quality control assessment of a product will be undertaken to ensure that it meets international quality requirements and is manufactured in compliance with good manufacturing practices (GMP).

The procedure for quality control 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 the finished product;
- Assessment of quality control units for compliance with good laboratory practices, as appropriate;
- Testing of product samples submitted.

Previous evaluation conducted by a National Medicines Regulatory Authority (NMRA) within the region may be taken into account during the evaluation conducted by WAHO.

## REFERENCES AND FURTHER INFORMATION

For further information on the WA-MRH regional Joint Medical Product Dossier Evaluation and Registration, please visit WAHO website at <https://www.wahooas.org> under the section **Resources**, sub-section **Publications and Research**, sub sub-section **Essential Medicines and Vaccines**.

**Deadline for the submission** of medicines dossiers to the Lead Coordinating NMRA (FDA-GH) is **Monday, 30 September, 2019 at 23:59 GMT**.