West African Health Organization
Promoting better health through Regional Integration

MPDER-MRH/EOI/21/008-03

WEST AFRICA MEDICINES REGULATION HARMONIZATION (WA-MRH) 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 HIV Infections and Related Diseases 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) under the section "WAHO Programs and Projects", sub-section "WA-MRH Project".

Assessment of product(s) submitted under this invitation will include evaluation of:

- a covering letter, expressing interest and confirming that the information submitted in the product dossier is complete and correct;
- product dossiers, which must include product data and information as specified in the guidelines for submission;
- each manufacturing site listed in the product dossier, must adhere to good manufacturing practices (GMP) in the required format specified in the ECOWAS Common Technical Guidance Documents for submitting a site master file;
- product samples, which must adhere to the requisite specifications.

If an evaluation demonstrates that the above four 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.

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.

LIST OF MEDICINES

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

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

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

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
- 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

HOW TO SUBMIT AN EOI

Applicants are strongly encouraged to contact the WAHO at the address: wahooas@wahooas.org and the Lead coordinating NMRA as early as possible to discuss specifics of the application. Applications are accepted from legal manufacturers. All manufacturers interested in submitting applications for review are requested to follow the steps below:

1. A pre-submission meeting (all interested applicants can attend) will be arranged by the coordinating NMRA for clarification on the technical requirements for their intended application submission in the 1st week of each submission window;
2. Contact of the Lead coordinating NMRA, email: akepaulakepaul@gmail.com, ake.ayodele@nafdac.gov.ng, tel: +234 (0)7038111573 to arrange for a meeting/call.
3. Please note that applications will not be accepted without prior consultation with Lead Coordinating NMRA.
4. Application letter would have to be submitted to the Lead Coordinating NMRA.

The Lead Coordinating NMRA for this invitation for EOI is the NMRA of Nigeria, the National Agency for Food and Drug Administration and Control (NAFDAC) (https://www.nafdac.gov.ng).

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 USD 500 for the lead coordinating NMRA (NAFDAC-Nigeria) for reception, screening, file

management and communication when submitting the file. The Bank account details are as follows:

Account Name:	CBN/NAFDAC GLOBAL FUND
Account Number:	100367-USD-CLBANK-60
Bank:	FBN BANK UK LTD
Address:	28 FINSBURY CIRCUS FBN BANK (UK) LTD, EC2M 7D LONDON, ENGLAND
Swift Code:	FBNIGB2L
IBAN:	GB94FBNI40520410036760

2. The applicant should download and complete the Market Authorization application (MA) file in accordance with the harmonized Common Technical Document (CTD) format in the WA-MRH project section under the Program and Projects at WAHO website (www.wahooas.org). The completed application MA file should be submitted electronically to the lead coordinating NMRA (registration@nafdac.gov.ng) with a hard copy sent to NAFDAC Office Complex, Plot 1, Isolo Industrial Estate, Oshodi-Apapa Expressway, Isolo, Lagos, Nigeria (telephone: +234 (0)7038111573).

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 WA-MRH Project section at the WAHO website. The samples should be submitted together with the Dossiers to the lead coordinating NMRA (NAFDAC-Nigeria).

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 USD 8,000
Applicants in other regions of Africa will pay USD 10,000
Applicants outside Africa will pay USD 12,000

The full fees for a product evaluation is USD 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 USD 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.

Product dossiers that have received WHO pre-qualification or other international regulatory authorities eg. The Food and Drug Authority of the United States (US-FDA) should be presented with evidence and the full package of the approved dossier by the institution.

REFERENCES AND FURTHER INFORMATION

For further information on the WA-MRH regional Joint Medical Product Dossier Evaluation and Registration, and Common Technical Document, please visit WAHO website at https://www.wahooas.org under the section Programs & Projects, sub-section WA-MRH Project.

Deadline for the submission of medicines dossiers to the Lead Coordinating NMRA (NAFDAC-Nigeria) is Friday, 19th November, 2021 at 23:59 GMT.