ECONOMIC COMMUNITY OF WEST AFRICAN STATES (ECOWAS)

WEST AFRICA MEDICINES REGULATORY HARMONIZATION (WA-MRH)
JOINT ASSESSMENT PROCEDURE FOR MEDICINE REGISTRATION AND MARKETING AUTHORIZATION OF MEDICINAL PRODUCTS

September, 2021
1. Background

Access to medicines is a key element of well-functioning health system. Availability and accessibility to medical products that meet international standards of quality, safety, and efficacy, is a key pillar for a responsive health system.

In West Africa, despite the concerted efforts of the Governments and Development Partners, the availability of quality medical products remains a major concern in most countries. Access to quality pharmaceutical products is inadequate because of various deficiencies related to poor governance and financing of the pharmaceutical sector, as well as weak regulatory capacity of the National Medicines Regulatory Authorities (NMRAs).

According to a NEPAD and WAHO Assessment in 2010-2011, the medicines regulatory systems in Sub-Saharan African countries are affected by fragmented legal framework, limited autonomy, lack of sustainable funding, poor infrastructure and institutional capacity, lack of cooperation amongst the authorities that are responsible for applying the Law, inadequate human resources, dependence on imported products, inadequate capacity of the Quality Control Laboratories to meet the requirements of the WHO Prequalification and lack of information sharing amongst the authorities.

All of these had resulted in cumbersome and non-transparent processes for medicine registration and lengthy registration timelines. This has imposed a huge demand on manufacturers when registering new medicines.

In order to overcome the challenges posed by the proliferation of illicit, substandard and falsified medicines, in 2014 the leadership of the West African Health Organization (WAHO) and West Africa Economic and Monetary Union (WAEMU) or “Union Economique et Monétaire Ouest-Africaine (UEMOA)”, agreed to strengthen their collaboration and stronger coordination in medicines regulatory harmonization (MRH) for the West Africa region. They further agreed that the Medicines Regulatory Harmonization (MRH) management for the entire ECOWAS region be under the oversight of WAHO. These initiatives include strengthening the local pharmaceutical industry, anti-counterfeiting strategies, support to capacity building initiatives of NMRAs and encouraging a dialogue for harmonization of medicines registration systems.

As part of implementation of provision of the WAHO Strategic Plan (2016-2020) and ECOWAS Regional Pharmaceutical Plan (ERPP), 2014-2020, WAHO/XVI.AHM/2015/Res-04/d. The WAHO Secretariat in collaboration with ECOWAS Member States National Medicines Regulatory Authorities (NMRAs) initiated the process of harmonizing requirements for the regulation of medicines through the legal mandate of the existing National Medicines Regulatory Authorities (NMRAs) in each of the Member States with the primary goal of increasing access to and affordability of safe, efficacious and good quality medicines in the region.

The Economic Community of West African States (ECOWAS) Medicines Regulatory Harmonization (ECOWAS-MRH) Initiative is implemented collaboratively by all the fifteen (15) NMRAs in the region.
The Heads of ECOWAS NMRAs resolved to form a WA-MRH Joint Steering Committee in February 2015 and proposed an approach for the West Africa Medicines Regulatory Harmonization project which was launched in November 2017 to be established under the frame work of the African Medicines Regulatory Harmonization (AMRH). They developed Term of References, a common Action Plan and Regulation, laid down ECOWAS procedures for the authorisation and control of medicinal products for human use and proposed the job description of future staff of the MRH Project Management Unit.

To make the implementation of the MRH initiative more effective a harmonized Common Technical Document (CTD) was developed in collaboration with WHO in line with international standards, validated and approved in June 2017 by the WA-MRH Steering Committee and being implemented by 15 member states as part of the overall harmonization of medicine regulation for Human Use. This CTD was adopted by ECOWAS Assembly of Health Ministers in March 2018.

In collaboration with WHO and partners, from 2017 to date, the regulatory functions of all 15 NMRAs in the region have been assessed using the WHO Global Benchmarking Tool. The regulatory capacities of NMRAs have been enhanced, with the Ghana Food and Drug Authority achieving WHO maturity Level 3 (ML3) in April 2020.

In March 2018, seven (7) Expert Working Groups for Medicines Evaluation and Registration, Good Manufacturing Practices (GMP), Quality Control (QC), Quality Management Systems (QMS), Information Management System (IMS), Pharmacovigilance and Clinical Trials (PV/CT), Policy, Legislation and Regulation were established. Each of these technical groups developed harmonized guidelines, requirements and standard operating procedures for Medicines Evaluation and Registration (MER), Good Manufacturing Practice (GMP), Quality Management System (QMS), Quality Control (QC), Pharmacovigilance /Clinical Trials (PV/CT), Information Management System (IMS) and Pharmaceutical Policy, Legislation and Regulation for both regional and national use. The documents were validated and approved by the WA-MRH Steering Committee in February 2019 to support the process.

Before the initiation of the joint regional registration process, the 15 NMRAs of member states of ECOWAS had different requirements for submission of dossiers for granting market authorization (MA) to medicines. In order to improve access to quality and safe medicines in the region, and within the framework of the West African Medicines Regulatory Harmonization (WA-MRH) Initiative, selected medicines in the regional basket will be authorized through the national authorization procedure, following a regional joint assessment procedure.

To accelerate the process, three (3) Lead Coordinating NMRAs were identified initially by the WA-MRH Steering Committee to work on rotation biannually, to receive, screen dossiers, assign evaluators, and manage communications with the applicants and the WA-MRH secretariat.

For the period June, 30 2021 to May, 31 2023, the Nigeria regulator NAFDAC will serve as the lead coordinating NMRA.
2. **Scope of products under the WA-MRH Joint Assessment Procedure**

The scope of medicinal products covered in the joint assessment procedure includes the following:-

a) Products on WHO’s Essential Medicine List).
b) Programme Medicines: (HIV/AIDS, Malaria, Tuberculosis, Reproductive Health, Neglected Tropical Diseases and Antibiotics).
c) Medicines used in Public Health Emergencies.
d) Products registered by Stringent Regulatory Authorities, prequalified by WHO, registered under Swissmedic MAGHP Procedure or EMA Article 58 (Positive Scientific opinion).
e) Life Saving Commodities (LSC) by the UN Commission on Life Serving Medicines for Women and Children.
f) Biological products (including Vaccines).
g) Blood products.
h) Medical Devices on a WAHO specific list to be published in the EOI.
i) Other priority medical products that WAHO will determine from time to time.

3. **General Joint Assessment Pathway**

3.1 **Joint Medicines Dossier Evaluation Procedure**

The Experts Working Group on Medical Products Dossier Evaluation and Registration (EWG-MPDER) has developed this WA-MRH joint evaluation procedure that has been endorsed by the Steering Committee of the WA-MRH initiative that includes all the heads of medicines agencies from the 15 ECOWAS countries.

There are eleven (11) steps under this procedure:

3.1.1 **STEP I: Expressions of Interest (EOI)**

- The WA-MRH secretariat launches an EOI for products eligible for joint evaluation listed in this procedure in Q4 of the preceding year for the next calendar year, indicating the four submission windows for the year, as well as the products eligible for each window.

- Each window will be open for a one (1) month period in each of the four (4) quarters of the year. The months for the four windows shall be February, May, July, and October.

- The invitation will be published on the WA-MRH Web-portal of WAHO website and other Partners websites.
• Product Dossiers are submitted to the Lead Coordinating NMRA.

• The coordinating NMRA (where the applications are submitted by the applicant) shall be stated in the EOI. A frequently asked questions guide will be made available on the WAHO and coordinating NMRA websites to guide potential applicants.

• By submitting an expression of interest, the applicant undertakes to share same information with all ECOWAS Member States’ NMRAs on all relevant aspects of quality, safety and efficacy of the specified medicinal products along with changes carried out and/or planned.

In situations of high public health concern as determined by ECOWAS Member States, the WA-MRH Secretariat at WAHO in consultation with ECOWAS Member States may directly invite relevant parties to submit specified products for assessment under this procedure without publication of an invitation for expressions of interest.

3.1.2 STEP II: Pre-submission meeting
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. After the pre-submission meeting, any new questions may be added to the FAQs guide and shared with all applicants who attended the meeting, as well as posted on the WAHO and coordinating NMRA websites.

3.1.3 STEP III: Submission and Dossier validation

3.1.3.1 Mode of Submission
• The dossier is submitted to the Coordinating NMRA by the applicant to the contact/address specified in the EOI.
• The dossier should be submitted in accordance with the validated ECOWAS CTD in electronic format (CD/DVD or USB flash drive).
• A payment of $500 (dossier validation fee) MUST be paid to the coordinating NMRA during the submission window or within 14 days after the closer of the window. Applications without a paid-up fee (and evidence of payment provided to the coordinating NMRA) in the specified timeframe will be considered non-compliant and will not be considered for the
window in question. Specific information on how to complete the payment (e.g. banking information) will be provided in the EOI.

- The Coordinating NMRA screens the dossier for completeness to determine the acceptability of the dossier for evaluation and issues Letter of Acceptability or deferral within a maximum of 15 days (from the date the payment is received) to the applicant.

- The dossier evaluation fee payment must be made to WAHO’s account (indicated in the EOI) within 14 days of the acceptance of the dossier by the Coordinating NMRA. Applicants are encouraged to make this payment at initial submission, or during the screening window to ensure that assessment can proceed immediately after the Coordinating NMRA has issued the Letter of Acceptability. The applicant will also share the Letter of Acceptability of the dossier with WAHO (via email wahooas@wahooas.org; cc: sossei@wahooas.org). The guide on the fee to be paid is provided in the EOI and can also be found at www.wahooas.org.

- This procedure is aimed to promote access to products by all the 15 ECOWAS countries. Applicants are encouraged to market the products in all 15 countries after they receive a regional recommendations.

WA-MRH Secretariat will identify an appropriate assessment team [two (2) assessors from two different NMRA’s or (1 member EWG-MPDER and 1 technical partner)] to evaluate a dossier where applicable.

3.1.3.2 Data and Information to be submitted to the Coordinating NMRA

c) A covering letter, expressing interest and confirming that the information submitted in the product dossier is complete and correct.

d) A product dossier, in the format specified in the ECOWAS Harmonized Common Technical Document (CTD) on Submission of Documentation for Registration of Human Medicinal Products.

c) Product and packaging samples, to enable visual examination and laboratory analysis.

d) A site master file for each manufacturing site listed in the product dossier, in the required format specified in the ECOWAS Common Technical Guidance Documents for submitting a site master file.
e) Evidence of payment to Lead Coordinating NMRA, and the WA-MRH Secretariat (may be paid on initial submission, however this must be received within 14 days after obtaining letter of acceptance from Lead NMRA following screening).

3.2 STEP IV: Technical Evaluation (Phase I)- Virtual
• The assessors (NMRA Assessors and the EWG member) evaluates in-country the allocated dossier(s) using the WA-MRH Technical Assessment Guide and generates a draft report (dossier comments and list of questions) within 45 days of the applicant submitting evidence of payment of region fee to WAHO. The report is uploaded on the WA-MRH Platform and WAHO secretariat notified.

3.3 STEP V: Joint Evaluation by EWG & Technical Partners: Face to Face/ Virtual (Phase I)
• The WA-MRH secretariat organizes joint assessment meeting 90 days after the close of each submission window for the EWG committee to peer review dossier comments and finalize list of questions to be sent to the applicant. The dates for the fours joint assessment sessions are here below:
  o Submission window #1 (February): Week 1 June
  o Submission window #2 (May): Week 1 September
  o Submission window #3 (July): Week 1 November
  o Submission window #4 (October): Week 1 February
• The Coordinating NMRA would notify the applicant(s) on the outcome of the joint assessment within 30 calendar days from the start of the joint assessment week or as follows:
  o Submission window #1 (February): on or before June 30
  o Submission window #2 (May): on or before September 30
  o Submission window #3 (July): on or before November 30
  o Submission window #4 (October): on or before February 28

3.4 Step VI: Joint GMP Inspection and Quality Control
• The WA-MRH secretariat organizes the Joint GMP Inspection and Quality Control of medicines in collaboration with the Coordinating NMRA after completion of the joint evaluation report (if recommended).
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✓ For Joint inspections refer to EWG Inspections guidelines.
✓ For samples schedule refer to EWG Quality Control guidelines.
✓ Samples are submitted at the same time as the application to the coordinating NMRA.
✓ The applicant has a maximum of 60 days to provide responses to the List of Questions that would be raised during the first Joint Assessment The response should be sent to coordinating agency (to the contact specified in the EOI). The Applicant can request for additional time in writing to the Coordinating NMRA.
✓ The Joint GMP Inspection and Quality Control go on at the same time.

3.5 STEP VII: Technical Evaluation Virtual (Phase II)
- The responses to the list of questions (LOQs) from the applicant are sent to the coordinating NMRA and uploaded to the WA-Platform for evaluation by the teams that assessed the initial dossier. The coordinating NMRA will send an email notification to the assessors.
- The assessment team will generate a draft report (technical report #2 addressing LOQs) within 15 days from the date the applicant responds to the LOQs. The report is uploaded at the end of the 15 days on the WA-MRH Platform and WAHO secretariat is notified.

3.6 Step VIII: Joint Evaluation by EWG & Technical Partners (Phase II): Virtual
- The WA-MRH secretariat organizes joint assessment to review technical report #2. LOQs are discussed at any of the EWG meetings between the four joint assessment sessions (see below) or at the four joint assessment session (whichever comes first). A maximum of 43 calendar days are allowed for technical report #2 to be tabled for discussion at any of these meetings. The EWG will prepare LOQs (if any) to be sent to the applicant. LOQs #2 shall be sent to the Coordinating NMRA within 7 days from the start of the EWG meeting. These meetings will run for 1-2 days each. Here are dates for the EWG meetings each year that address LoQs:
  - EWG meeting #1: Week 3 July
  - EWG meeting #2: Week 1 October
  - EWG meeting #3: Week 1 December
EWG meeting #4: Week 1 April

- The Coordinating NMRA would notify the applicant(s) on the outcome of the joint assessment within 5 days after the end of the 2nd joint assessment.

3.7 Only applications with not more than 2 major queries (issues that may pose serious risk to public health, and that affect overall approvability of the product – not administrative issues) as determined by the EWG will be allowed to go into the phase III for supplementary evaluation. Step IX: Technical Evaluation Phase 3

- The responses to the LOQs #2 from the applicant are sent to the coordinating NMRA within 30 days of receiving them from the Coordinating NMRA; responses will be forwarded to the WA-Platform for evaluation by the EWG and the assessment team with 7 days of receipt and discussed at the immediate next joint evaluation session (allow 30 days regulator’s time max).

3.8 Step X: Final Joint Evaluation by EWG & Technical Partners: Virtual

- The WA-MRH secretariat includes the responses to the LOQ #2 received from the Lead Coordinating NMRA on the agenda of the next joint evaluation session or meeting of the EWG for final decision. A final report is produced within 14 days from the start of the final joint review meeting.

The WA-MRH Secretariat is notified by the Chair of the EWG-MPDER about the completion of the joint evaluation process. The report is communicated to the WA-MRH Secretariat by the Chair of the EWG-MRH.

4.0 WHO Collaborative Assessment Pathway

1.1 Collaborative Assessment Procedure:

- This is a procedure for collaboration between the WHO Prequalification of Medicines Programme (WHO/PQP) and WA-MRH in the assessment and accelerated joint registration of WHO prequalified pharmaceutical products.
• In this procedure, WA-MRH would voluntarily agree to implement this collaborative procedure and accept the task of processing applications for registration of WHO-prequalified pharmaceutical products in accordance with the terms of the Procedure.

• A list of participating authorities including ECOWAS Member States’ NMRAs is posted on the WHO/PQP web site (http://www.who.int/prequal/).

• The duration of the process from submission of the application to the Coordinating NMRA until final WA-MRH Steering Committee recommendation under the Joint Assessment Procedure should take 60 days if a complete and high standard dossiers are fully submitted. (figure 2)

5.0 Step XI: Validation by WA-MRH Steering Committee:
• The report is presented to the WA-MRH Project Steering Committee by the Chair of the EWG-MRH for validation (30 days allowed).

• The Coordinating NMRA notifies the recommendations of the Steering Committee to the manufacturer within a period of 7 days after the approval of the Steering Committee. The notification is valid for 2 years.

• The Coordinating NMRA sends also at the same time the final report, the electronic record and recommendations to each country.

The meetings of the Steering Committee will be held at the following times:
  o Steering Committee meeting #1: Week 4 of July
  o Steering Committee #2: Week 4 of October
  o Steering Committee #3: Week 4 of February
  o Steering Committee #4: Week 4 of April

The duration of the process from submission of the application to the Coordinating NMRA until final WA-MRH Steering Committee recommendation under the Joint Assessment Procedure should take ~120 calendar days (for a complete dossier that receives no queries), and 226 calendar days with a single round of list of questions. (figure1)

6.0 Reporting and communication of the results of assessment
• The team of assessors will finalize its report from the joint assessment session according to the established ECOWAS SOP and format, describing the findings and including recommendations and issues to communicate to applicant, manufacturer(s) and/or testing unit(s) or organization(s), where relevant.

• The ECOWAS EWG for Dossier Assessment reserve the right to terminate the procedure of assessment of a specific product the applicant is not able to provide the required information within six months and no written request for extension of time has been submitted.

• In the event of any disagreement between an applicant and WA-MRH assessment, an SOP established by the WA-MRH for the handling of appeals and complaints will be followed to discuss and resolve the issues.

• The WA-MRH Steering Committee shall be entitled to use and publish public assessment reports, subject to the protection of any commercially confidential information of the applicant, manufacturer(s) and/or testing organization(s).

7.0 Outcome of Joint Assessment Procedure

• Once the WA-MRH Steering Committee is satisfied that the assessment process is complete for the relevant product, and that the WA-MRH harmonized requirements and standards are met, the product, as produced at the specified manufacturing site(s), a notification letter on completion of assessment of the dossier will be issued by the WAHO Secretariat to the applicant/manufacturer.

• The letter shall state that the final recommendation for registration outcome will be communicated by WAHO Secretariat, subject to compliance to all the requirements.

8.0 Maintenance of registration status

The list and details of recommended products shall be maintained in WA-MRH along with information about individual NMRA registration subject to:-

• Continued compliance with requirements of quality, safety and efficacy

• Payment of retention fees in accordance with respective WA-MRH’s Fees
• The Market Authority Holder (MAH) communicates details to WAHO Secretariat of any changes (variations) made to the registered product following the ECOWAS harmonized guidelines on variations to a registered product.

• The MAH applies for renewal of their products in accordance with ECOWAS Guidelines on Procedural Aspects for registration of medicinal products.

• Continued GMP compliance of the manufacturing site(s).

• Continued compliance with Medicines Health Policies and any other directives.

**Note**

In the course of assessment all measures will be taken to ensure that confidentiality of the information submitted is protected by all participating Parties.

**9.0 National Autorisations:**

• Based on the notification, the applicant has a maximum period of 2 years to apply for Marketing Authorisation (MA) across the ECOWAS countries.

• The competent authority (DG, NMRA or Minister of Health) delivers the Marketing Authorization (MA) within a maximum period of 60 days after the applicant has filed with the NMRA the specific product, the accompanying WAHO notification of recommendation, and the relevant local requirements including national fees. (figure3)

• This procedure will give marketing authorization in ECOWAS Member State(s);

• The Marketing Authorization Holder (MAH) can begin to make the medicine available to patients and healthcare professionals in ECOWAS Member States where marketing authorization has been granted.
Figure 1:
THE WEST AFRICAN MEDICINES REGULATORY HARMONIZATION (WA-MRH) JOINT EVALUATION PROCEDURE
Figure 2:

Current Plan of Submission Process (ECOWAS)-Reliance
Figure 3:

National procedure for processing a drug registration application

- **NMRA RECEIPT OF APPLICATIONS FOR MA**
- **NMRA/ADMINISTRATIVE ANALYSIS**
  - Regional approved product
  - National Process product
    - Incomplete Dossier
    - Complete Dossier
      - Renewal & Minor variation
      - New application/Major Variation

- **Committee of experts**
- **NATIONAL DRUG REGISTRATION COMMISSION**
  - REJECTED
  - ACCEPTED
  - ADJOURNED
    - Letter of notification of the decision of the National Drug Registration Commission
      - Ex gratia or contentious appeal
      - MA Proposal to the Minister of Health
      - ask for any additional information