WEST AFRICAN HEALTH ORGANIZATION (WAHO)

REGIONAL JOINT ASSESSMENT PROCEDURE FOR MEDICINE REGISTRATION AND MARKETING AUTHORIZATION OF MEDICINAL PRODUCTS

July, 2019

Introduction

Access to medicines is a key element of well-functioning health system. The availability and accessibility of medical products that are of acceptable quality, safety, and efficacy, are very important to make a responsive health system that can overcome the challenges facing public health.

In West Africa, despite the concerted efforts of the Government 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 of the pharmaceutical sector and 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 the 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 Agencies.

All of these have resulted in cumbersome and non-transparent processes for medicine registration and insufficient regulatory capacity to approve medicines for sale in a timely manner. 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 circulating in the region, and to improve the accessibility of quality, safe and efficacious 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 control 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, namely West Africa Medicines Regulatory Harmonization (WA-MRH) Initiative.

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) and Global Medicines Regulatory Harmonization (GMRH). 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. CTD has since March, 2018 been adopted by ECOWAS Assembly of Health Ministers.

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 Trails (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.

- The present pathway was developed by an Expert Working Group for Medical Product Dossier Evaluation and Registration (EWG-MPDER) in May, 2019.

1. Procedures for Marketing Authorization (MA) in the WA-MRH

Currently, the West Africa has no Regional Medicines Regulatory Agency, which has legal mandate for marketing authorization of medicinal products. In view of this, 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, after the joint assessment procedure.

1.1 National authorization procedure

1.1.1 Each ECOWAS Member States has its own procedures for the authorization of medicines, within their own territory, that fall outside the scope of the joint assessment procedure. Information about these national procedures can be found on the website of the National Medicine Regulatory Authority (NMRA) in the country concerned.

1.1.2 This procedure will give marketing authorization in ECOWAS Member State(s).

2. Joint Medicines Dossier Evaluation Procedure

2.1.1 This is a procedure for joint assessment by the Expert Working Group on Medical Products Dossier Assessment of the selected medicinal products, inspection of their respective manufacturing site(s) followed by Steering Committee approval of jointly accepted medicinal products.

2.1.2 If the assessment of medicinal products dossier is successfully completed and jointly accepted, the ECOWAS Member Sates NMRAs will grant marketing authorization within maximum of three (3) months from the date of joint acceptance.

2.1.3 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.

2.2 WHO Collaborative procedure

2.2.1 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.

2.2.2 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/).

3. 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) WAHO's assessment of the priority health needs in the region;

b) WHO's evidenced-based treatment guidelines (WHO Essential Medicine List);

c) Programme Medicines: (HIV/AIDS, Malaria, Tuberculosis, Reproductive Health, Neglected Tropical Diseases, Vaccines);

d) Medicines used in Public Health Emergencies;

e) Products registered by Stringent Regulatory Authorities, prequalified by WHO, registered under Swissmedic MAGHP Procedure or EMA Article 58 (Positive Scientific opinion);

f) Life Saving Commodities (LSC) by the UN Commission on Life Serving Medicines for Women and Children.

4. Mode of application in the WA-MRH Joint assessment procedure

4.1 Invitation of Expression of Interest (EOI)

4.1.1 At least twice a year and/or as needed, EWG on MPED under WA-MRH will review the scope and list of products invited under expression of interest. The updated invitation of expression of interest will be published on the WA-MRH Web-portal of WAHO websites.

- WA-MRH secretariat launches EOI for eligible medical products for a period of 1 month.
- Product Dossiers are submitted to the Lead Coordinating NMRA.

4.1.2 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.

4.1.3 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.

4.2 Data and Information to be submitted

4.2.1 Applicant should submit both soft and hard copies of the product dossier(s) with the required information to the Lead Coordinating NMRA.

4.2.2 In submitting an EOI for medicinal product evaluation, the applicant should send to Lead Coordinating NMRA.:-

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

b) 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 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.

4.2.3 Fees to be paid by the applicants to the WA-MRH Secretariat will continue as by regional registration fees regulations.

4.3 Screening of Dossiers submitted

4.3.1 Each product dossier submitted by an applicant will be screened within two weeks by a Lead Coordinating NMRA in medicines evaluation and registration for completeness.

4.3.2 In the event the dossier is incomplete, the applicant will be informed and requested to complete the dossier.

4.3.3 Dossiers that are considered complete as the result of the administrative screening will be submitted to MRH Expert Working Group in medicines evaluation and registration.

- Once admissibility has been established, the lead coordinating NMRA issues the applicant with an admissibility certificate and informs the WA-MRH Secretariat within a maximum of **7 days**;

- The lead coordinating NMRA post the files on a platform to be accessed by assessors within 7 days after notification by WA-MRH Secretariat.

4.4 Dossier Assessment

4.4.1 The assessment will be done by Experts Working Group, in accordance with ECOWAS Standard Operating Procedure (SOP) for joint assessment.

4.4.2 WA-MRH joint assessments will be concluded within a period of three months from the date of acceptance of an application.

4.4.3 Dossier assessment shall be done concurrently with GMP and if applicable, GLP and GCP inspections.

4.4.4 After review of the assessment report, a face to face meeting will be convened to finalize the reports of the joint assessment. The outcome of the assessment will be shared with WA-MRH Steering Committee for insight and the applicant informed by the Secretariat.

4.4.5 If any additional information is required, applicants will be required to provide such additional information to the WA-MRH Secretariat within 60 days, and any extension beyond the specified period should be justified. If no written responses are received within 60 days from the date indicated on the letter, it will be deemed that you have withdrawn the application.

4.4.6 Experts Working Group will postpone its decision of the acceptability of the respective product dossier, until such information has been evaluated and found satisfactory in light of the specified standards.

4.4.9 Upon receipt, the responses to the queries shall be assessed within two months by the Experts Working Group on Medicines Evaluation and Registration.

4.4.10 Technical support and expertise from WHO, Stringent Regulatory Authorities, any other technical experts in the area, may be sought in the process of dossier assessment.

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

4.5 Site Inspection

Site(s) inspection shall be conducted in accordance with the ECOWAS procedure for conducting GMP inspections

4.6 Reporting and communication of the results of assessment

4.6.1 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.

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

4.6.3 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.

4.6.4 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).

4.7 Outcome of Joint Assessment Procedure

4.7.1 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.

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

4.8 Maintenance of registration status

The registered products shall be maintained in WA-MRH and each NMRA's list of registered products subject to:-

4.8.1 Continued compliance with requirements of quality, safety and efficacy.

4.8.2 Payment of retention fees in accordance with respective WA-MRH's Fees.

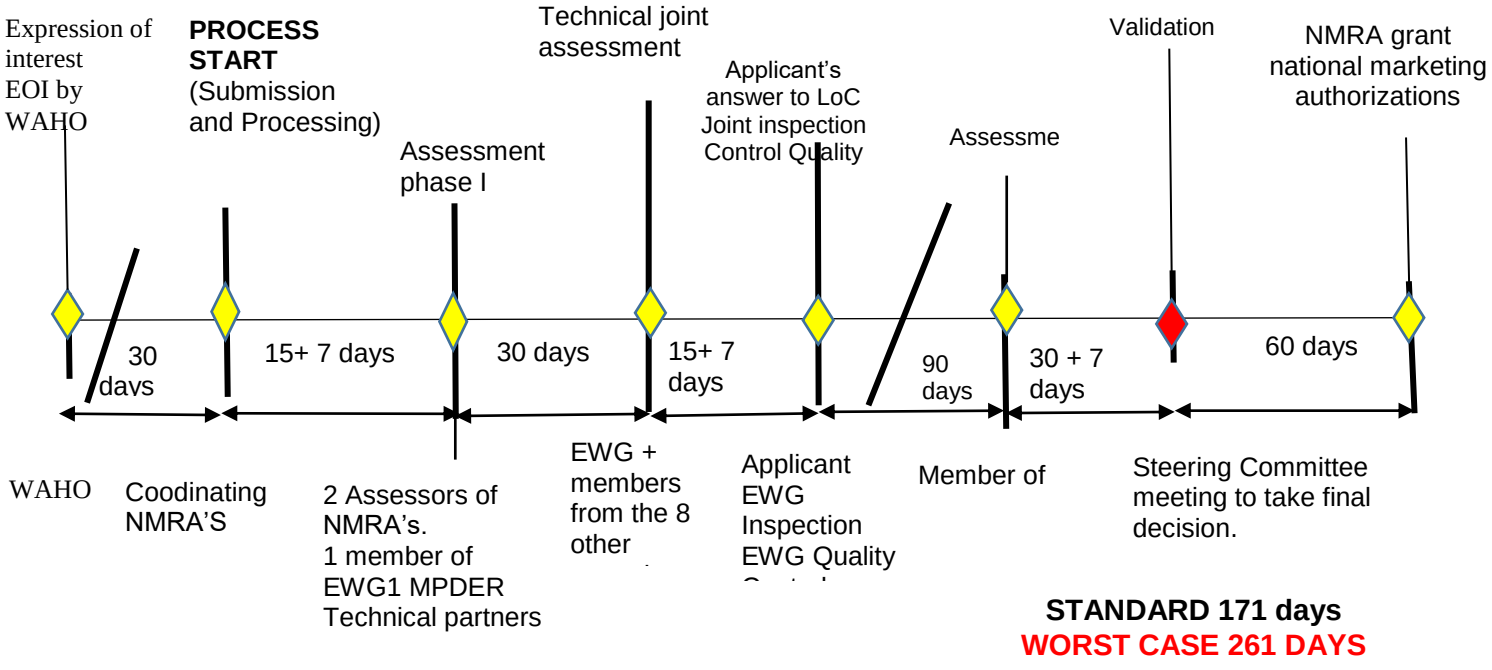
4.8.3 The MAH communicates details to WAHO Secretariat of any changes (variations) made to the registered product following the ECOWAS harmonized guidelines on variations to a registered product.

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

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

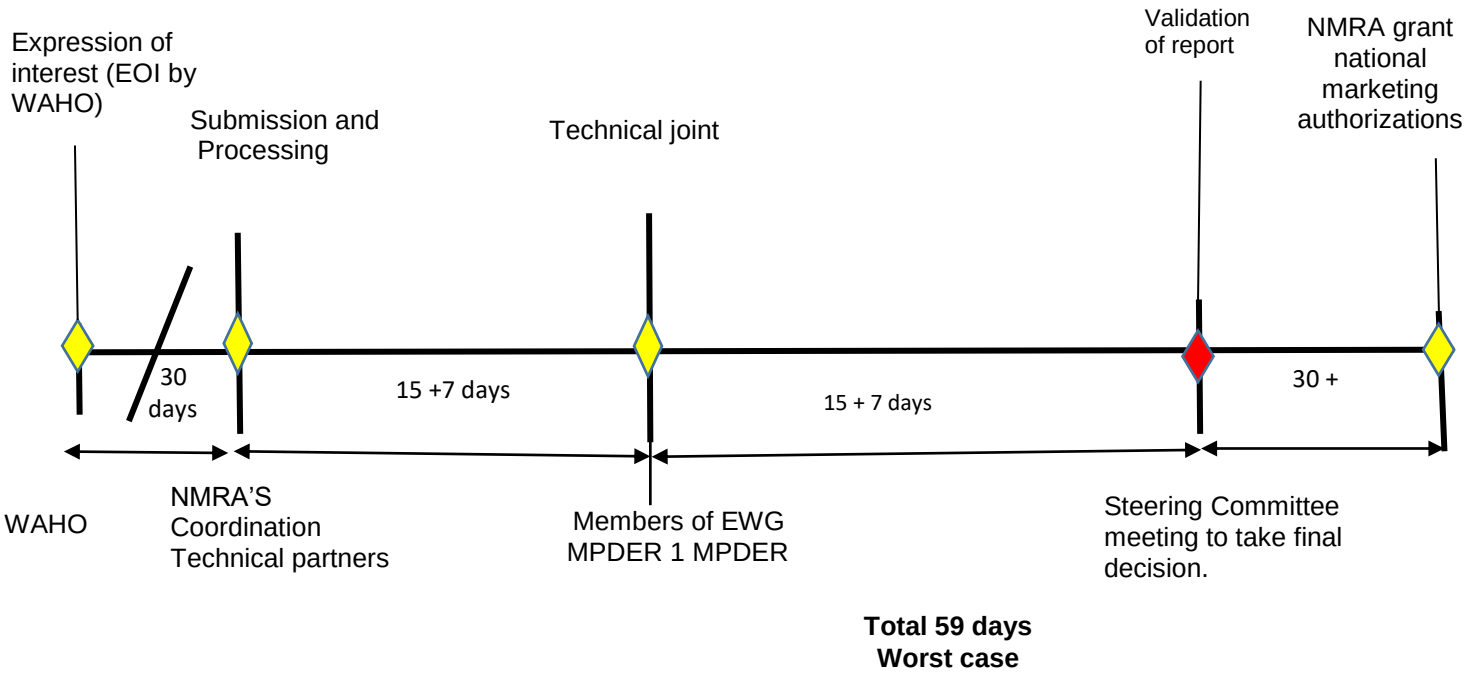
4.8.6 Continued compliance with Medicines Health Policies and any other directives.

General Pathway for Medical Products Joint Submission Procedure in ECOWAS



STANDARD 171 days
WORST CASE 261 DAYS

COLLABORATIVE PROCEDURE IN ECOWAS WITH TECHNICAL PARTNERS



Notification of the advice /recommendations should be sent to the manufacturer.

NB: This notification is valid for 2 years and is non-renewable.

- Stop clock system used.

National approval:

- After the applicant has submitted the file in the country, the final report is presented for consideration by the internal committee or the National Commission for a final decision.

- The National Commission shall meet within a maximum period of **30 days** after the applicant has submitted the file in the country. A copy of the decision is sent to the MRH Secretariat for information. The market authorization (MA) notification must be made within **30 days** of notification of the final decision.

- TOTAL DAYS = **171** Calendar days (Worst case: **261** days).