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 2022

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 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 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 framework 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 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.

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 February 29 2024, 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 EOI for products eligible for joint evaluation listed in this procedure **is opened all year round.**

- **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) is compulsory for new chemical entities to the region while for existing chemical entities should be based on request. The meeting would be arranged by the lead coordinating NMRA for clarification on the technical requirements for their intended application submission. 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.

3.1.3.2 **Data and Information to be submitted** to the Coordinating NMRA

a) A covering letter, stating purpose 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) Applicant to provide the Leaflet insert, SmPC, Artwork, Pictorial of the secondary and primary packaging material and product

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

e) 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.

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).

3.1.3 STEP III: Submission and Dossier validation (Screening)

3.1.3.1 **Mode of Submission**

- A payment of $500 (dossier validation fee) **MUST** be paid to the coordinating NMRA within 14 days of indication of interest 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. Specific information on how to complete the payment (e.g. banking information) will be provided in the EOI.
- The dossier is submitted to the **Coordinating NMRA** by the applicant using the upload link provided by the lead NMRA.
- The dossier should be submitted in ECOWAS CTD format.
- 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 thirty (30) days (from the date the payment is confirmed) to the applicant. (NB: the 30 days is not inclusive of the applicant's response time, a maximum of 2 responses allowed after which a re-submission attracts a re-screening fee of $500)

3.1.4 STEP IV – DOSSIER EVALUATION

- The dossier evaluation fee payment must be made to WAHO's account indicated in the letter of acceptance issued by the Coordinating NMRA within fourteen (14) days. Applicants are encouraged to make this payment at initial submission, or during the screening to ensure that assessment can proceed immediately after the Coordinating NMRA has issued the Letter of Acceptability. 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 fifteen (15) ECOWAS member countries. Applicants are encouraged to market the products in all fifteen (15) countries after they receive the regional recommendations.
- WA-MRH Secretariat in collaboration with the chairman of the EWG will identify and confirm the availability of the selected assessor in the country to evaluate the dossier.

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 Forty-Five (45) **days** post confirmation of payment and assignment of dossier to the selected NMRA**.** The report is uploaded on the WA-MRH Platform.

3.3 STEP V: Joint Evaluation by EWG & Technical Partners: Face to Face/ Virtual (Phase I)

- The WA-MRH secretariat organizes joint assessment meeting within twenty-one (21) days of the upload of the technical report for peer review comments and finalize the list of questions to be sent to the applicant as applicable.
- The Coordinating NMRA would notify the applicant(s) on the outcome of the joint evaluation within Seven (7) days after the meeting

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).

NB

- ✓ *For Joint inspections refer to EWG Inspections guidelines.*
- ✓ *For samples schedule refer to EWG Quality Control guidelines.*
- ✓ *Samples are to be submitted immediately after the acceptance of the dossier(s) by the coordinating NMRA.*
- ✓ *The applicant has a maximum of ninety (90) 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 with justification for the extension.

- ✓ *The Joint GMP Inspection and Quality Control go on at the same time where applicable.*

3.5 STEP VII: Technical Evaluation Virtual (Phase II)

3.5.1 The responses to the list of questions (LOQs) from the applicant are sent to the coordinating NMRA for evaluation by the selected NMRA, after confirmation of availability.

3.5.2 The assessor will generate a draft report (technical report #2 addressing LOQs) within twenty (20) days from the date of the assignment of the additional data The report is uploaded within three (3) days of completion of the report.

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 submitted by the assessor within thirty (30) days of upload of completed technical report (TR2). The EWG will prepare LOQs (if any) to be sent to the applicant by the lead NMRA within 7 days of the completion of the EWG joint evaluation meeting.

- The responses to the LOQs #2 from the applicant are sent to the assessor(s) for further review and steps 3.5.2 and 3.6 above are repeated.
- NB: If dossier is found unacceptable after the third round of assessment (after second LOQ response), any re-submission will attract 50% of the original charge.

3.7 Step IX: Joint Evaluation by EWG & Technical Partners: Virtual

If dossier is satisfactory the EWG will prepare final report for consideration by the steering committee and inform the WA_MRH secretariat of same within fourteen (14) days after the EWG meeting

4.0 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/ratification within thirty (30) days of submission to the secretariat by EWG Chair

- The applicant is notified of the regional decision not more than fourteen (14) days after the meeting of the steering committee. The notification is valid for 2 years.
- The Coordinating NMRA would make available final report, t, QIS and notification of approval to all member countries through the WAHO portal for ease of access and reference.

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 ~133 calendar days (for a complete dossier that receives no queries), and 196 calendar days with a single round of list of questions. (figure1)

5.0 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 ninety (90) days 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).

6.0 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.

7.0 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 revalidation 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

8.0 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.

9.0 WHO Collaborative Assessment Pathway

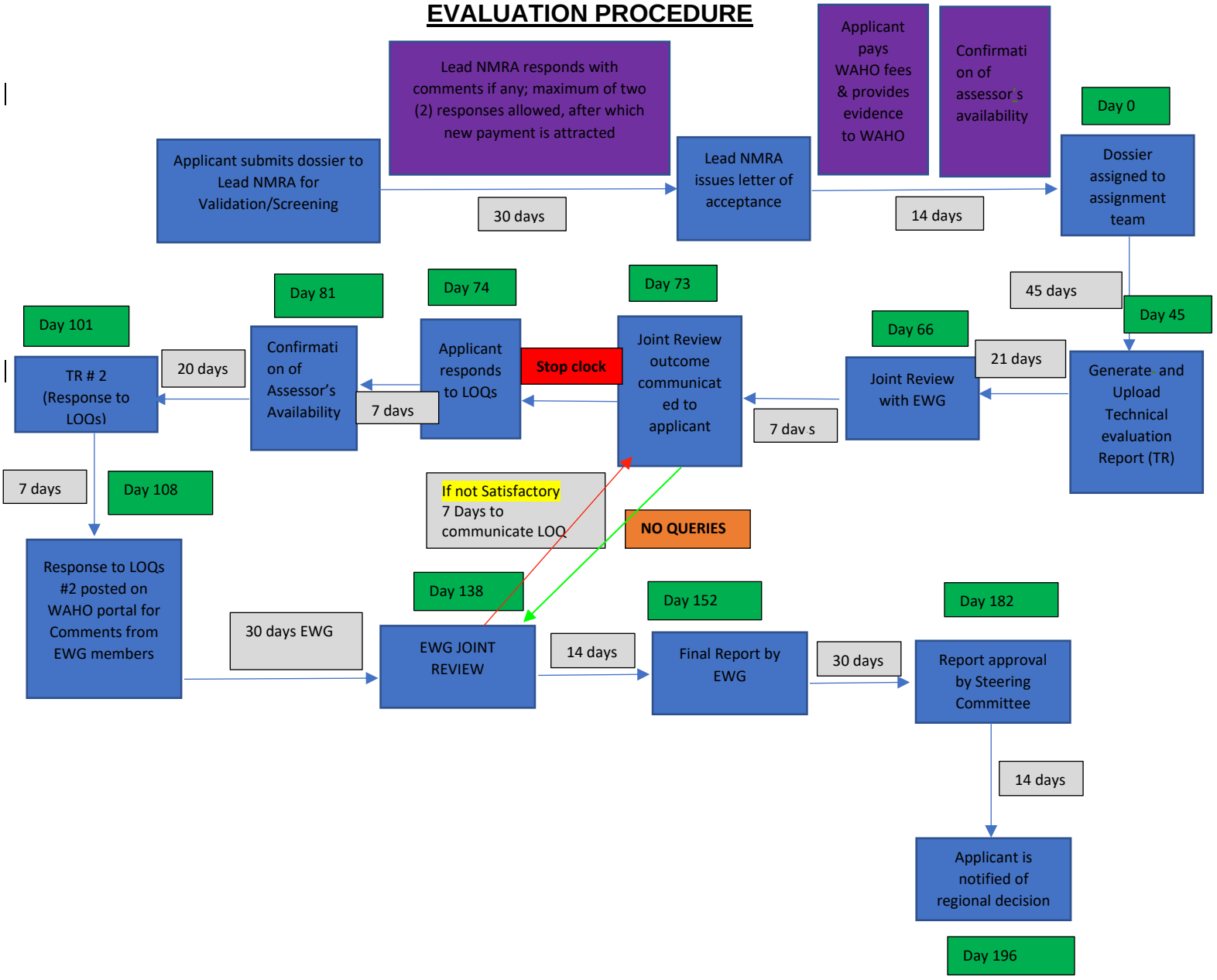
1.1 Collaborative Assessment Procedure:

- 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 complete and high standard dossiers are fully submitted. (figure 2)

Figure 1:

THE WEST AFRICAN MEDICINES REGULATORY HARMONIZATION (WA-MRH) JOINT EVALUATION PROCEDURE



THE WEST AFRICAN MEDICINES REGULATORY HARMONIZATION (WA-MRH) JOINT EVALUATION PROCEDURE FOR RELIANCE

Figure 2:

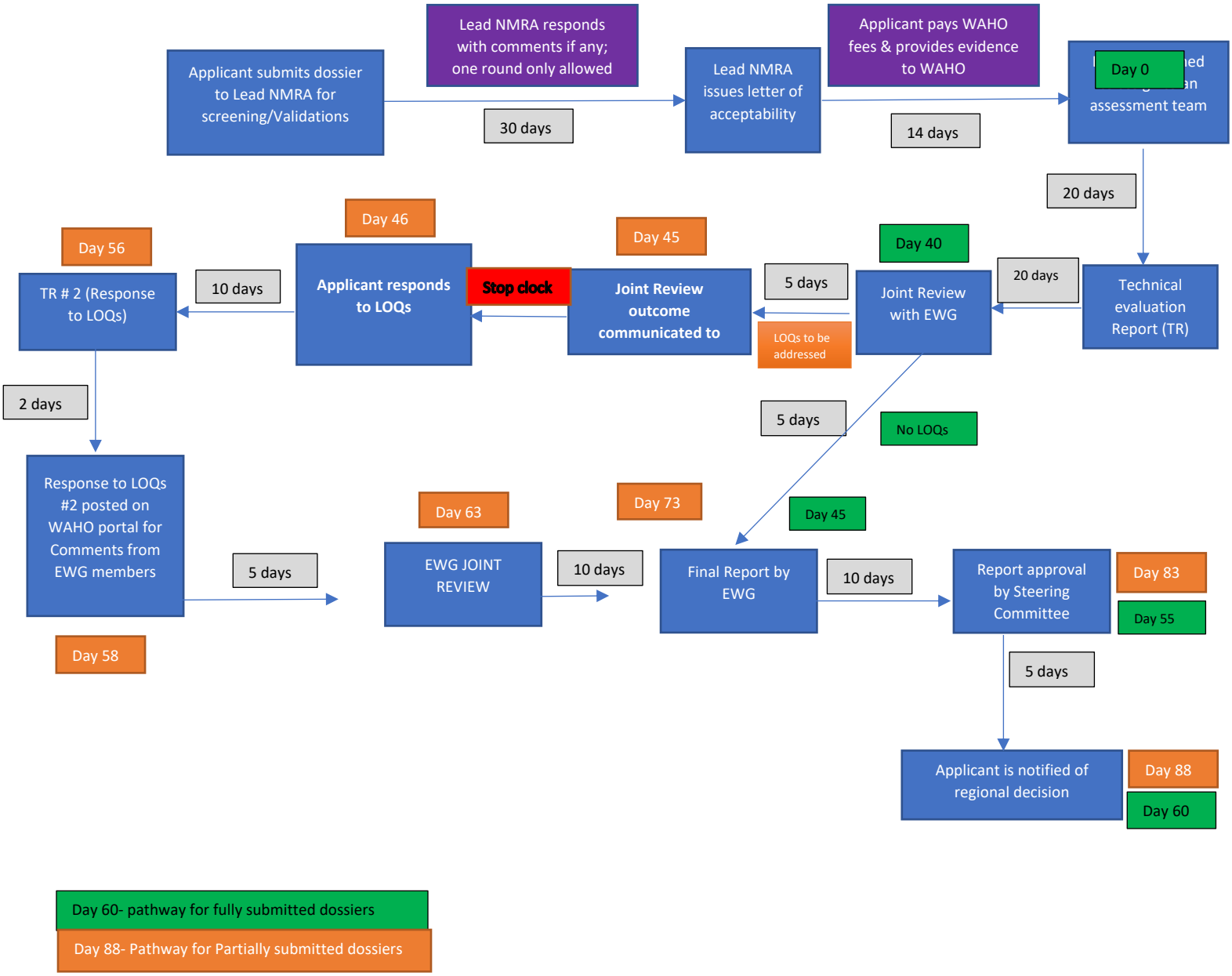
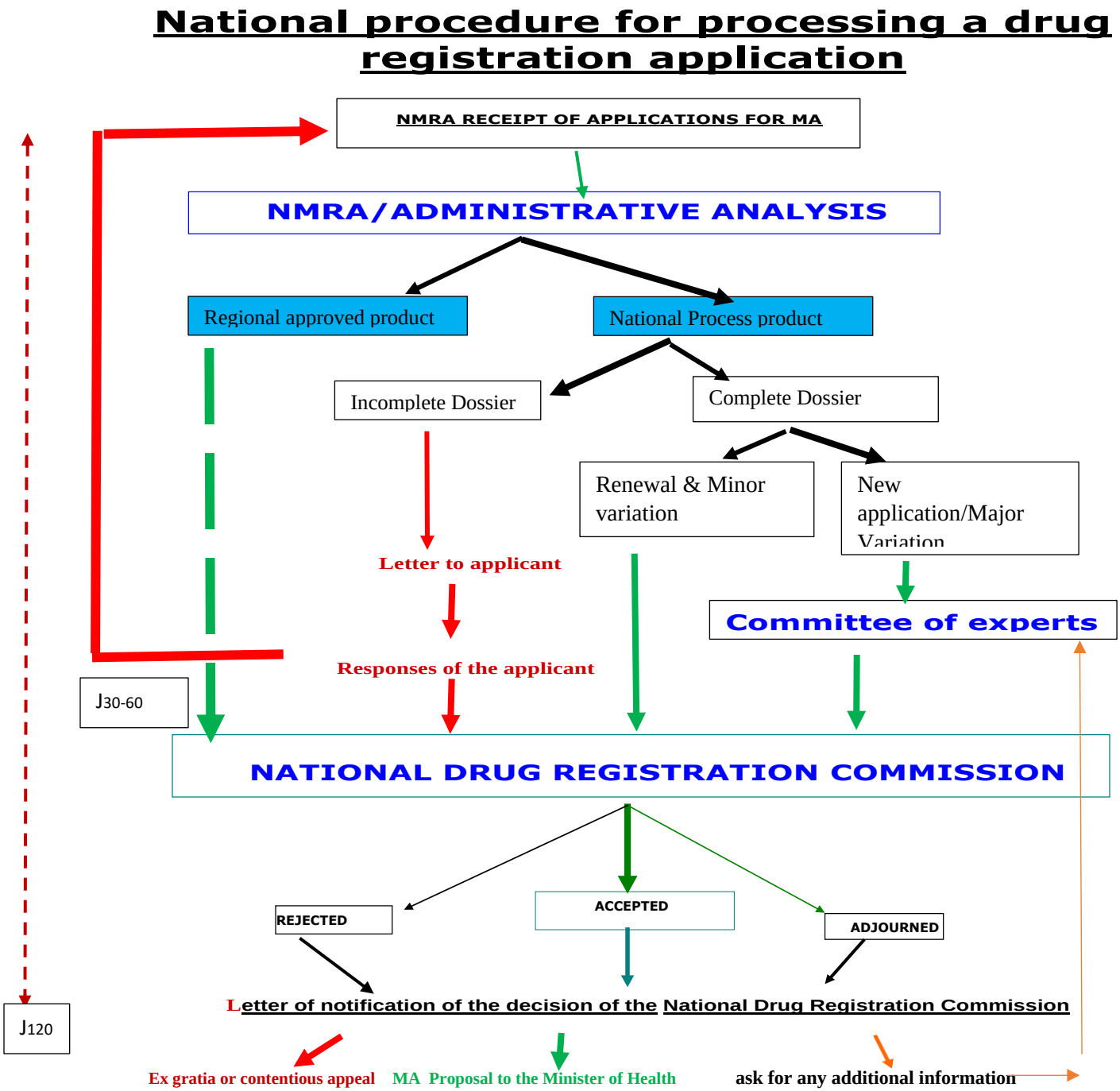


Figure 3:


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
Letter to applicant
Committee of experts
Responses of the applicant
J30-60
NATIONAL DRUG REGISTRATION COMMISSION
REJECTED
ACCEPTED
ADJOURNED
Letter of notification of the decision of the National Drug Registration Commission
J120
Ex gratia or contentious appeal
MA Proposal to the Minister of Health
ask for any additional information