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Translated from French

Subregional Programme for the Harmonization of National Pharmaceutical Policies in Central Africa (Central African Economic and Monetary Community)

Framework for Joint Evaluations of Applications for Marketing Authorizations in the Central African Economic and Monetary Community

Preface

The Harmonization of National Pharmaceutical Policies (HNPP) programme in the Member States of the Central African Economic and Monetary Community (CEMAC) began in 2007 with the development of a Common Pharmaceutical Policy (CPP).

Since its adoption at a high Community level, as established by Supplementary Act No. 07/13-CEMAC-OCEAC-CCE-SE-2 of the Conference of CEMAC Heads of State of 14 June 2013, the effective implementation of the CPP has been entrusted to the Organization of Coordination for the Control of Endemic Diseases in Central Africa (OCEAC) which, in its capacity as CEMAC's Executive Agency for health issues, oversees the coordination and monitoring of all programmes and projects aimed at translating this important subregional integration tool into health policy.

The four priority areas identified and described in the CPP document as requiring continuous improvement and monitoring include the quality assurance of medicines through the establishment of effective approval; pharmacovigilance and pharmaceutical inspection systems; and the provision of resources to ensure the systematic control of medicinal products in circulation in the CEMAC region.

In that context, the following normative documents were adopted as Community Regulations and form the basis of CEMAC's pharmaceutical regulatory framework:

- Community Regulation No. 03/13-UEAC-OCEAC-CM-SE-2 on guidelines for pharmacovigilance;
- Community Regulation No. 04/13-UEAC-OCEAC-CM-SE-2 on the manual of pharmaceutical inspection procedures;
- Community Regulation No. 02/13-UEAC-OCEAC-CM-SE-2 on the adoption of guidelines for the provision of essential medicines;
- Community Regulation No. 05/13-UEAC-OCEAC-CM-SE-2 on the harmonization of procedures for the approval of medicines for human use in the CEMAC region.

OCEAC welcomes the fact that the CPP has been developed with the involvement of all CEMAC Member States and partners, including the African Union Development Agency-New Partnership for Africa's Development (AUDA-NEPAD), the World Health Organization (WHO) and the World Bank, to all of which I am sincerely grateful.

This framework for joint evaluations of applications for marketing authorizations (MAs) for medicinal products in the CEMAC region sets out the terms and conditions for the organization of and procedure for joint evaluations, and the responsibilities they entail.

The implementation of this framework by all CEMAC Member States will ensure that medicines in circulation throughout the CEMAC subregion are of identical quality. The OCEAC Executive Secretariat will do its utmost to ensure that the process of issuing MAs no longer restricts the availability of medicines, so that people can access high quality essential medicines in a timely manner.

The Executive Secretariat of OCEAC urges the national regulatory authorities (NRAs) in the six CEMAC Member States to adopt the procedure, and counts on their full participation in the monitoring mechanisms that will be implemented at the Community level.

Lastly, the Executive Secretariat wishes to thank all technical and financial partners for supprting initiatives to harmonize pharmaceutical policies in the CEMAC region and for the organization of joint evaluation sessions for applications for MAs, in particular those for medicines and other health products.

Dr Khadidja Guirsimi Youssouf

Executive Secretary

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Abbreviations

MA	marketing authorization
NRA	national regulatory authority
GMP	good manufacturing practices
CEMAC	Economic and Monetary Community of Central Africa
CTD	Common Technical Document
EMA	European Medicines Agency
FDA	Food and Drug Administration
HNPP	Harmonization of National Pharmaceutical Policies
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
OCEAC	Organization of Coordination for the Control of Endemic Diseases in Central Africa
WHO	World Health Organization
CPP	Common Pharmaceutical Policy
ToR	Terms of Reference

Definitions

- **Marketing authorization (MA)**: an official document issued by a competent pharmaceutical regulatory authority for the marketing or free distribution of a product, following an evaluation of its safety, efficacy and quality.
- **National regulatory authority (NRA)**: a national body or structure responsible for implementing pharmaceutical regulatory functions, including the approval of medicines and other pharmaceutical products.
- **Good manufacturing practices (GMP)**: that part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization.
- **Quality control**: the sum of all the tests and assays conducted in the laboratory to ensure that a pharmaceutical product complies with specified quality standards.
- **Applicant/applicant laboratory**: a manufacturer or its authorized representative applying for approval of a medicinal product for human use.
- **Fees for joint evaluations of applications**: fees payable by the applicant for the technical evaluation of the application dossier for a marketing authorization, conducted by the Expert Committee. The fees are to be paid in one sum, into the bank account designated by the Community.
- **Harmonization fees**: fees payable by the applicant for the issuance of a marketing authorization in a Member State. The fees are paid by each country in accordance with national regulations.
- **Inspection**: an official examination conducted by the competent authorities on the premises and/or in institutions, to ensure compliance with applicable regulations and standards.
- **Medicine**: any substance or combination of substances presented for treating or preventing disease in human beings or which may be administered to human beings with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions.

1. Introduction

The main objective of the CPP adopted by CEMAC Member States is to help improve access to health services by making safe, effective and high quality pharmaceutical products available to the entire population at minimal cost. To achieve this, the six CEMAC Member States — Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea and Gabon — have undertaken to draft, adopt and implement common procedures for the approval of medicinal products in the countries of the CEMAC region, based on a set of harmonization standards; to establish a technical approval committee in all CEMAC Member States; and to promote the mutual recognition of approvals issued by CEMAC Member States, on the basis of an identical reference system for evaluation.

Despite the adoption in 2013 of Community Regulation No. 05/13-UEAC-OCEAC-CM-SE-2 on the harmonization of procedures for the approval of medicines for human use, registration remains an enormous challenge, limiting the availability of medicinal products. Many innovative medicinal products, and even high quality generic medicines, are slow to enter the markets where they are most needed, either because they are not registered in time or because the MA expires before renewal. This creates a void likely to be filled by falsified or inferior products.

To address this situation, CEMAC Member States have agreed to implement collaborative evaluation activities for applications for MAs. This process began in 2015 with the technical support of partners. Three in-person joint evaluation sessions were held in Gabon, Chad and Cameroon in April 2019, October 2019 and March 2024 respectively. Several other sessions were held in a virtual format. These joint evaluations were conducted in accordance with a procedure adopted by CEMAC Member States in 2017.

In view of the difficulties encountered in implementing the procedure, a new framework for conducting joint evaluations in the CEMAC region was proposed and approved by Member States following a consultant review commissioned by OCEAC in partnership with the World Bank.

The framework for joint evaluations of medicines in the CEMAC region is based on Community Regulation No. 05/13-UEAC-OCEAC-CM-SE-2 on the harmonization of procedures for the approval of medicines for human use, which was adopted by CEMAC Member States in 2013. It ensures the reliability and sustainability of joint evaluations, which have a direct impact on the quality of the medicines available to the populations of countries in the CEMAC region. It is part of the pan-African African Medicine Regulatory Harmonization (AMRH) programme led by AUDA-NEPAD and WHO, and is aligned with the guidelines of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).

2. Objective of joint evaluations of applications for marketing authorizations for medicinal products in the CEMAC region

The objective of joint evaluations of applications for MAs by all experts from Member States is to improve the availability of high quality medicines in the CEMAC region by accelerating the evaluation process and strenthening the robustness of the technical analysis of application dossiers.

3. Principles of joint evaluations

Joint evaluations are based on three fundamental principles:

- Pooling of technical expertise;
- Adoption at the national level of the regional technical report on the evaluation of applications for MAs; and
- Building the capacity of the NRAs.

4. Organization of joint evaluations

The NRAs in the CEMAC region have opted for a centralized system for the submission and monitoring of applications for MAs. This system — which differs from that used in the other regional economic communities of the African region (the Southern African Development Community, the East African Community, and the Economic Community of West African States) but is similar to that used by the European Medicines Agency (EMA) and WHO — facilitates the introduction of the mutual recognition of MAs, as advocated by the CPP. It also makes it possible to bridge the gaps between the NRAs and facilitate capacity building and, more generally, the harmonization of procedures. The centralized procedure means that manufacturers need not apply to the NRAs in their countries of interest or for each medicine of interest, because a rigorous process will be implemented ensuring that the medicines in circulation in the region are of identical quality.

This mechanism is structured around two main bodies: the Technical Secretariat and the Expert Committee.

(a) Technical Secretariat

The Technical Secretariat for joint evaluations of applications for MAs operates under the auspices of the Executive Secretary of OCEAC. It is responsible for managing the joint evaluation process, in particular by operating the platform for the submission of dossiers, and by sharing information, monitoring approvals, organizing technical evaluation sessions and providing support to the NRAs.

Its principal functions are to:

- Ensure the implementation of the framework for joint evaluations;
- Select candidate dossiers for joint evaluation;
- Conduct an administrative evaluation of these dossiers;
- Send candidate dossiers to the expert conducting the evaluations;
- Monitor the quality control of samples using an accredited laboratory;
- Draft the Terms of Reference (ToR) for each of the technical sessions for joint evaluation;
- Ensure that the draft call for expressions of interest is provided to the Executive Secretary of OCEAC by the deadline, together with the eligibility criteria for candidate dossiers;

- Oversee the operation of the platform to be established for the submission of candidate dossiers;
- Act as a liaison between the experts conducting the evaluations and the pharmaceutical laboratories holding the candidate dossiers, in particular when additional information is requested by the experts;
- Monitor the implementation of recommendations made by the experts and the NRAs, in particular the adoption of decisions at the regional and national levels;
- Ensure communication between the members of the Technical Working Group for Approval;
- Ensure the logistical organization of joint evaluation meetings;
- Send to the applicant laboratory the final technical assessment report on its candidate dossier;
- Request the Technical Working Group for Inspection to conduct a good manufacturing practices (GMP) inspection of the manufacturing site of the candidate medicinal product, if necessary;
- Ensure that the inspection report on the manufacturing site is sent to the Expert Committee for consideration as part of the assessment process; and
- Make any relevant recommendations.

The Technical Secretariat is composed of representatives from the NRAs of the six CEMAC Member States.

Members of the Technical Secretariat must be pharmacists working in the department responsible for the approval of medicinal products in the NRAs of CEMAC Member States, and must be appointed by the minister for health of the country concerned.

Members are required to declare any apparent, potential or real conflict of interest arising from their membership of the Technical Secretariat.

Participation in the meetings of the Technical Secretariat is not remunerated. However, members receive a fixed allowance from the fees paid by pharmaceutical laboratories at the regional level, prior to the joint evaluation sessions.

(b) Expert Committee

The Expert Committee is composed of 18 members from CEMAC MemberStates with recognized expertise in the fields of pharmacology, galenic pharmacy or pharmaceutical technology; therapeutic chemistry or pharmaceutical chemistry; clinical or hospital pharmacy; toxicology; clinical biochemistry; biology (bacteriology, mycology, parasitology, virology and haematology); cardiology; paediatrics; internal medicine; neurology; care of the elderly; renal medicine; oncology; hepatology and gastroenterology; immunology; vaccinology; infectious disease; and gynaecology.

The experts are nominated by the NRA in their country of origin in response to a call for applications, and are then selected by the Executive Secretariat of OCEAC on the basis of their curriculum vitae.

The function of the Executive Committee is to:

- Conduct a scientific and technical evaluation of applications for MAs in one or more CEMAC Member States; and
- Make any relevant recommendations aimed at maintaining the quality of medicinal products in circulation in the CEMAC region.

In exercising that function, it is the responsibility of the Expert Committee to:

- Pool experts' preliminary evaluations of candidate dossiers;
- Compile a list of the information to be requested from the applicant laboratory by the Technical Secretariat, if necessary;
- Review the report provided by the Technical Secretariat of the site inspection conducted by the Technical Working Group for Inspection;
- Review the quality control results provided by the Technical Secretariat for the candidate product;
- Prepare the joint technical evaluation reports to be sent to the NRAs;
- Approve the final joint technical evaluation report to be sent to the Technical Secretariat; and
- Make any relevant recommendations aimed at maintaining the quality of medicinal products in circulation in the CEMAC region.

The reports of the meetings of the Expert Committee are submitted to the heads of the NRAs for review and approval. The final report is sent to the Technical Secretariat for submission to the Executive Secretary of OCEAC, as well as to the applicant laboratories and the NRAs.

Members of the Expert Committee are required, before undertaking their duties, to declare any apparent, potential or real conflict of interest arising from their membership by signing a confidentiality undertaking declaring any conflicts of interest.

They are paid a fee for their expertise, the amount and terms of which are set by the Executive Secretary of OCEAC.

5. Scope of joint evaluations

Priority classes of medicines have been defined in a mutual agreement between OCEAC and Member States. Any manufacturer wishing to place a medicinal product belonging to these classes on the CEMAC market, regardless of the number of target countries, must make use of the joint evaluation procedure.

The range of products, which is limited initially, may be expanded over time as experience is acquired.

The priority classes of medicines are:

Category 1:

- New chemical or biological entities (originator medicines), including improved traditional medicines;

- Complex generic products (i.e. products with complex active ingredients, formulations, dosage forms or routes of administration, or drug-device combination products and liposomal forms); and vaccines and other biological products such as biotherapeutic

products and similar biotherapeutic products (biosimilars), including gene therapies and advanced gene therapies.

Category 2:

- Medicines designed to treat priority diseases identified in African populations, such as non-communicable diseases (NCDs), neglected tropical diseases (NTDs), and metabolic diseases.

6. Procedure for joint evaluations

The procedure for joint evaluations of applications for MAs in the CEMAC region has three phases:

Phase 1: Call for expressions of interest

1. The Executive Secretary of OCEAC will launch a call for expressions of interest for the placing on the CEMAC market of medicines belonging to the priority categories identified jointly by OCEAC and the Member States.

2. The applicant laboratory prepares its candidate dossier in the Common Technical Document (CTD) format, in accordance with Appendix 2 of Community Regulation No. 5/13-UEAC-OCEAC-CM-SE-2 on the harmonization of procedures for the approval of medicines for human use in the CEMAC region, which is available on the OCEAC website (www.oceac.org).

3. Applications must be submitted in a sealed envelope marked “CEMAC Joint Evaluation Application” to the approval department of one of the NRAs in the CEMAC region, within 90 days of publication of the call for expressions of interest.

The sealed envelope must also contain an electronic version of the candidate dossier on a USB stick.

Samples of the products and reference substances must be submitted at the same time as the candidate dossier. The samples provided must conform to the provisions of Appendix 3 of Community Regulation No. 5/13-UEAC-OCEAC-CM-SE-2 on the harmonization of procedures for the approval of medicines for human use in the CEMAC region, which is available on the OCEAC website (www.oceac.org).

Phase 2: Administrative evaluation of dossiers

The Technical Secretariat will conduct an administrative evaluation of the application dossier to confirm its acceptability in accordance with the provisions of Appendix 4 of Community Regulation No. 5/13-UEAC-OCEAC-CM-SE-2 on the harmonization of procedures for the approval of medicines for human use in the CEMAC region, which is available on the OCEAC website (www.oceac.org), and will provide the applicant with notification of acceptability or non-acceptability within 15 days of the close of the call for expressions of interest.

For each dossier accepted, the applicant must pay the joint evaluation fee into OCEAC’s bank account (details below) within 15 days of receipt of notification.

BANK: SOCIETE COMMERCIALE DE BANQUE CAMEROUN (SCB CAMEROUN)

ACCOUNT NAME: HPPN/CEMAC REGULATIONS

BANK CODE: 10002

SORT CODE: 00069

ACCOUNT NUMBER: 90001728553

RIB KEY: 19

IBAN: CM2110002000699000172855319

BIC: BCMACMCX

Calls for expression of interest will specify the amount of the joint evaluation fees for pre-selected application dossiers. These fees will be used to conduct technical and scientific evaluations of the dossiers.

The fees applicable at the regional level differ significantly from those at the national level (assuming that the procedure continues and culminates in the issuance of an MA).

If an applicant receives notification of non-acceptability, another application for an MA may be submitted for pre-selection in a future call.

Phase 3: Technical evaluation of dossiers

A technical and scientific evaluation of the application dossiers provided by the Technical Secretariat is conducted by members of the Expert Committee.

The number of experts and their profiles will be determined by the Technical Secretariat on the basis of the dossiers to be evaluated.

The aim of the evaluation is to ensure that the product meets international quality requirements and is manufactured in accordance with GMP.

The evaluation includes, but is not limited to:

- A general understanding of the manufacturer's production and quality control activities;
- An evaluation of the data and information provided by the manufacturer on the safety, efficacy and quality of the product, including its formulation, manufacturing and test data and results;
- An evaluation of the manufacturing site's compliance with GMP and of the consistency of the production and quality control of raw materials, with a particular focus on active pharmaceutical ingredients and the final product;
- An evaluation of quality control units to ensure compliance with good laboratory practices, where appropriate;
- Testing of submitted product samples.

The period for the evaluation of the dossiers by experts may not exceed 30 days.

Once the expert evaluation has been completed, the Technical Secretariat will hold an initial meeting of the Expert Committee. The person responsible for approval at each NRA will be invited to this meeting, which will be organized in accordance with the prevailing rules of CEMAC.

The experts will appoint a chair and a rapporteur for the meeting, and will discuss the application dossiers submitted and any issues arising from their review. A preliminary report will be prepared and sent to the Technical Secretariat, together with any questions requiring clarification and any other comments, for the attention of the requesting laboratory.

The applicant will have 60 days to respond to the clarifications requested by the Expert Committee and transmitted by the Technical Secretariat. Once this deadline has passed, the Technical Secretariat will note the absence of a response and will deem the application to have been rejected.

The clarifications will be reviewed by the experts, who will then prepare their report. This will be examined at a second meeting of the Expert Committee organized by the Technical Secretariat and attended by the heads of the NRAs in the six CEMAC Member States. The meeting will culminate in the approval of the experts' conclusions by the NRAs, and the adoption of the expert report specifying whether the medicinal product has all the necessary qualities to be placed on the CEMAC market.

The Technical Secretariat will send applicant laboratories a report on the joint evaluation of their application dossier.

The entire joint evaluation process, from the close of the application window to the sending of reports to applicants, is expected to take 135 days (not including the 60 days for applicants to provide clarifications).

7. Adoption of the regional technical report at the national level

The issuance of MAs is the responsibility of the NRA in each Member State. Following receipt of the joint evaluation report, the applicant must follow the registration procedure in the target CEMAC Member State(s) with a view to registering the medicinal product(s). However, this procedure will be simpler and quicker than usual, as the product will already have been the subject of a technical evaluation.

The manufacturer shall send to each country of interest a dossier consistent with that submitted for the joint evaluation (Appendix 2 of Community Regulation No. 5/13-UEAC-OCEAC-CM-SE-2 on the harmonization of procedures for the approval of medicines for human use in the CEMAC region, which is available on the OCEAC website (www.oceac.org)), together with the report of the joint evaluation conducted at the regional level.

The applicant must pay the approval fees, in accordance with the regulations in force in the country concerned.

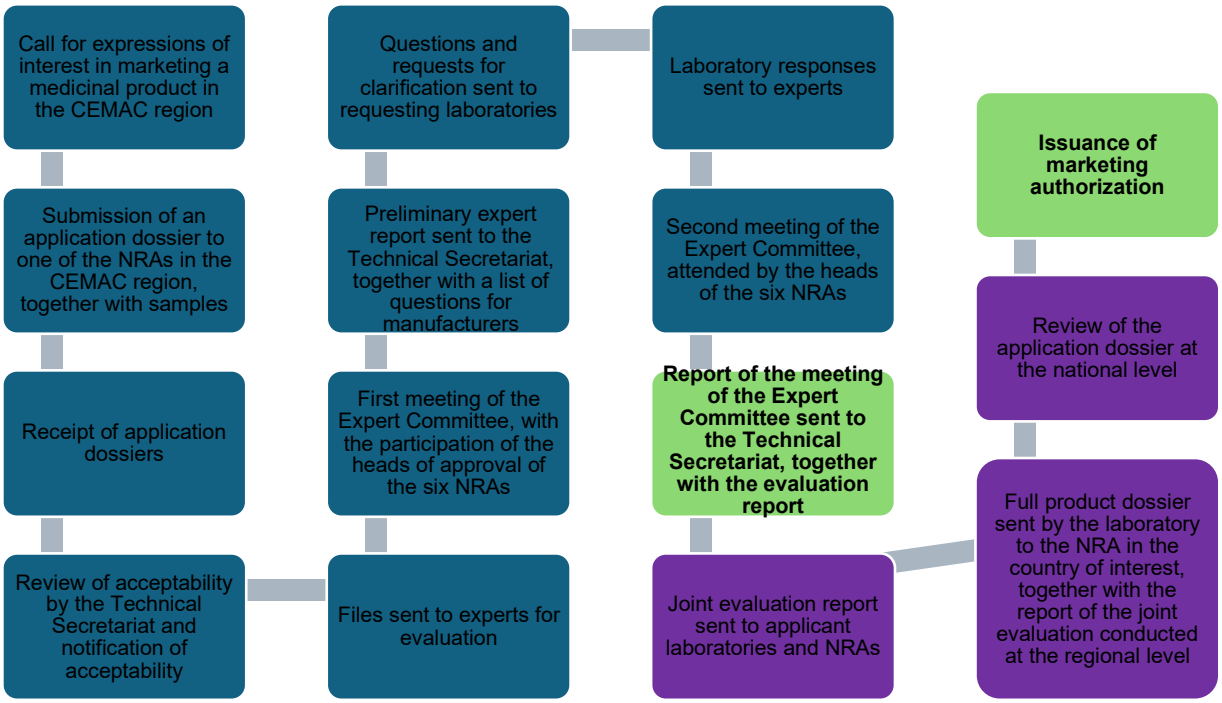
The review of the dossier at the national level does not constitute a second evaluation of the product, but will instead focus on questions of 'sovereignty'.

Following the adoption of the joint evaluation technical report at the Community level, any refusal of approval at the national level cannot be justified on technical or scientific grounds and must be notified to the Technical Secretariat.

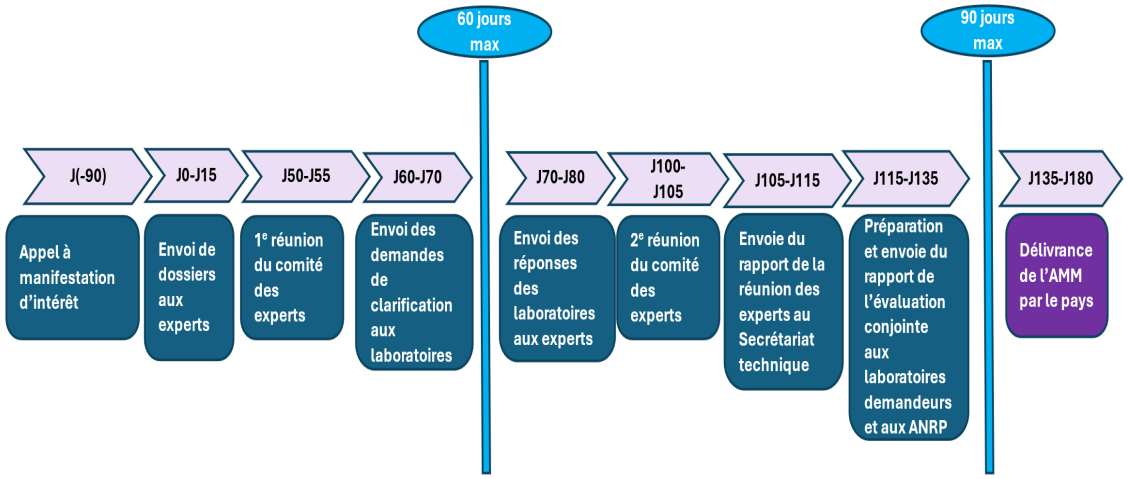
The Technical Secretariat will monitor applications for MAs in CEMAC Member States and ensure that MAs are issued within 45 days.

Appendices

Appendix 1: Procedure for joint evaluations of applications for marketing authorizations



Appendix 2: Timetable for joint evaluations of applications for marketing authorizations



Soit un total de 180 jours entre le dépôt à l'OCEAC et la délivrance de l'AMM par le pays

Day (-90) – Call for expressions of interest
Day 0-15 – Application dossiers sent to experts
Day 50-55 – First meeting of the Expert Committee
Day 60-70 – Requests for clarification sent to laboratories

60 days maximum

Day 70-80 – Laboratories' responses sent to experts
Day 100-105 – Second meeting of the Expert Committee
Day 105-115 – Report of the Expert Committee meeting sent to the Technical Secretariat
Day 115-135 – Joint evaluation report prepared and sent to applicant laboratories and NRAs

90 days maximum

Day 135-180 – Issuance of MA by the country concerned

I.e. a total of 180 days from the submission of the application to OCEAC and the issuance of an MA by the country concerned.