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Public guidance

Parallel application for EU-M4all (Article 58) opinion and Centralised Marketing Authorisation procedure

Promoting EU-Medicines4all

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Summary

Article 58 of Regulation (EC) No 726/2004 provides that the European Medicines Agency (EMA) may give a scientific opinion for medicines intended to be used outside the European Union, primarily for low- and middle-income countries (LMICs). This work is done in cooperation with the World Health Organization, and with regulators and experts from third countries where the medicines are intended to be used. It is now called EU Medicines for All or EU-M4all.

The EU-M4all procedure has demonstrated its ability to have real public health impact as the scientific opinions from the Committee for Medicinal Products for Human Use (CHMP) of EMA have been used for numerous marketing authorisations across the world. It has also contributed to increased collaboration of the European Union in the field of public health, particularly with Sub-Saharan African countries.

Since the introduction of the procedure in 2004, a number of medicines have received a positive EU-M4all opinion. Some of them also have received a centralised European marketing authorisation (MA), obtained before or after the EU M4all opinion.

In addition to the EU-M4all procedure exclusively intended for third-country markets, the EMA is now offering the possibility to run the evaluation of **centralised and EU-M4all applications in parallel**, to obtain an EU-M4all Scientific Opinion and a Centralised Marketing Authorisation at about the same time.

This initiative offers opportunities for work-saving and reduced duplication of efforts since most elements of the CHMP scientific advice and assessment for the centralised procedure and EU-M4all are the same.

For applications evaluated under this initiative, WHO experts and experts/observers nominated by WHO from target countries act as scientific expert reviewers to the rapporteurs' assessment reports and provide specific expertise and input, as for a standalone EU-M4all procedure.

General criteria for a parallel assessment

To meet the criteria for a parallel EU-marketing authorisation application (MAA) and EU-M4all assessment, the active substance(s) of both applications must be identical and the product information must be comparable¹. EMA expects that both procedures are submitted by the same applicant.

The technical dossier of the intended medicines shall be identical. Differences such as different formulations, pharmaceutical forms, storage conditions or routes of administration should be discussed with the Agency before the submission to determine whether they are compatible with a parallel assessment.

As for any other initial MAA, eligibility for both procedures should be ideally requested at the same time to EMA; EMA recommends providing the eligibility request preferably at the earliest 18 months, and at the latest 7 months, before the MAA/EU-M4all applications are submitted to the EMA.

At time of filing, two separate eCTD submissions are required and cross-referencing to the other application is not allowed. Two separate validations of application will be performed before the start of the procedures.

The dossier requirements for an EU-M4all application are mostly the same as for the [centralised procedure](#) with a few important differences, as reflected in the ['EMA procedural advice for medicinal](#)

¹ Some sections of the product information may differ slightly to reflect the context of use *in the target countries*. If significantly different with differences in the non-clinical and clinical parts of the submission, then the benefits of 'parallel' assessment are deemed to be minor. In such cases, it will be more appropriate to conduct two fully independent assessments.

[products intended exclusively for markets outside the European Union under Article 58 of Regulation \(EC\) No 726/2004 in the context of co-operation with the World Health Organisation \(WHO\)](#)'.

The applicant should identify the differences between the two dossiers with regard to quality, non-clinical and clinical aspects at pre-submission. Any differences in Modules 1-5 should be reflected in their submissions (e.g. in a comparative table annexed to Module 1).

Applicants are strongly advised to request early Scientific Advice and to present their proposal and dossier content at the EMA pre-submission meeting, at least 6-7 months before the intended submission date.

Following validation, and if the parallel assessment meets the required criteria, both applications should follow the same timetable and be assessed in parallel. Whilst two CHMP ARs and Opinions will be adopted, one for each procedure, common document will be envisaged during the evaluation where relevant (e.g. a joint List of Questions). It is to be noted that the applications will start with the same timetable, however during the assessment the procedural timetables may differ (e.g. in case of delays in submission of responses, change in the timetable of one application from accelerated to standard timelines). The benefit of having the same CHMP/PRAC rapporteurs to perform the review is recognised.

Unlike for the EU-MAA, after the adoption of the CHMP scientific opinion for an EU-M4all medicine, there is no European Commission decision.

In the pre- and post-opinion phases, EU-M4all can be subject to Good Manufacturing Practices (GMP) Good Laboratory Practices (GLP), Good Clinical Practices (GCP) and pharmacovigilance inspections, as for a centralised product.

Clinical trials submitted as part of EU-M4all applications must be conducted in accordance with GCP, independently of the circumstances (e.g. country, population, data collection) under which they are performed. Based on previous cases where EU-M4all clinical trials were performed in challenging conditions, applicants are highly encouraged to share an overview of actual GCP compliance in early discussions such as Scientific Advice and/or pre-submission meetings.

In the post-opinion phase the EU-M4all scientific opinion needs to be kept up to date. The opinion holder should inform EMA of any changes concerning their medicine ([post-authorisation guidance](#)) by submitting relevant [variations](#), [periodic safety update reports](#) (PSURs) and other post-opinion applications as for a centralised product. The opinion holder must also fulfil the pharmacovigilance requirements agreed with EMA.

EMA applies the [same fees as for the centralised marketing authorisation procedure](#). However, in exceptional cases, applicants can request a total or partial fee waiver from EMA's Executive Director. The request for fee waiver should be submitted as early as possible and not later than 3 months before applying for scientific advice or submitting the application.

For further information please check the public guidance on:

-[Pre-authorisation guidance](#)

-[Post-authorisation guidance](#)

-[Obtaining an EU marketing authorisation](#)

-[Obtaining and maintaining a scientific opinion on an EU-M4all medicine](#)