EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Public guidance

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

Promoting EU-Medicines4all

Draft finalised by EMA	October 2020
Start of public consultation	14 January 2021
End of consultation (deadline for comments)	15 February 2021

Comments should be included in the form published with this draft guidance and should be sent to EMAInternational@ema.europa.eu by 15 February 2021.

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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 the LMICs 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, 11 medicines have received a positive EU-M4all opinion. Five of them also have (or have had) a centralised European marketing authorisation (MA). Four of these medicines obtained the centralised authorisation before the EU-M4all opinion, one after the EU-M4all opinion.

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 about the same time.

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

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 intended indication(s) must be comparable[1]. EMA expects that both procedures are submitted by the same applicant.

Concerned medicines may have different formulation, pharmaceutical forms, storage conditions or routes of administration. This means that the intended medicines must be chemically/biologically and clinically identical but can be physically distinct.

As for any other initial MAA, eligibility for both procedures should be requested to EMA at the earliest 18 months before submissions and, at the latest 7 months before the MAA/EU-M4all are filed with 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 both applications 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 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)'.

[1] Indications may differ slightly to reflect the context of use. If indications differ significantly then the benefits of a 'parallel' assessment are deemed to be minor with significant differences in the non-clinical and clinical parts of the submission. In such cases, it will be more appropriate to conduct two fully independent assessments.

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. with a comparative table annexed to Module 1).

Applicants are strongly advised to present their proposal and dossiers content at the EMA pre-submission meeting at least 6-7 months before the intended submission date.

Following validation and should the parallel assessment meet the required criteria, both applications should follow the same timetable and be assessed in parallel. 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. delays in submission of responses). The benefit of having the same CHMP/PRAC rapporteurs to perform the review is recognised.

Unlike the EU-MAA, after the adoption of the CHMP scientific opinion for an EU-M4all product 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.

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 an 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