16 January 2023
EMA/119843/2013 Rev 17*
Human Medicines Division

Information package for certificates of medicinal products issued by the European Medicines Agency (EMA)

Table of contents

**Amended and added text in revision 17 (16 January 2023) appears in Italic.*

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

1. Introduction

The purpose of a certificate of a medicinal product (CMP) is to confirm the marketing authorisation status of the medicinal product and that the medicinal product is produced in accordance with Good Manufacturing Practice (GMP) standards.

CMPs are issued in the framework of the World Health Organisation (WHO) certification scheme on the quality of pharmaceutical products moving in international commerce. According to such a scheme, the CMP is intended for use by the competent authority within an importing country when the product in question is under consideration for a product licence that will authorise its importation and sale and when administrative action is required to renew, extend, vary or review such a licence.

The procedures for authorisation and, consequently, certification of medicinal products in the European Union (EU) are complex. The objective of this document is to provide a brief and understandable summary of the arrangements. More detailed information is available in the appropriate EU legislation[1,2,3].

2. Authorisation of medicinal products in the EU/EEA

The EU Member States are:

Belgium, Bulgaria, Czechia, Denmark, Germany, Estonia, Ireland, Greece, Spain, France, Croatia, Italy, Cyprus, Latvia, Lithuania, Luxembourg, Hungary, Malta, Netherlands, Austria, Poland, Portugal, Romania, Slovenia, Slovakia, Finland, Sweden and United Kingdom (Northern Ireland).

For the UK, as from 1.1.2021, EU Law applies only to the territory of Northern Ireland (NI) to the extent foreseen in the Protocol on Ireland/NI.

Norway, Iceland and Liechtenstein form the European Economic Area (EEA) together with the Member States of the EU. These countries have, through the EEA agreement, adopted the complete EU acquis on medicinal products and are consequently parties to the EU procedures. Where in this document reference is made to Member States of the EU this should be read to include Norway, Iceland and Liechtenstein.

In the EEA, both the European Commission and the national health authorities can authorise medicinal products. Medicinal products authorised by the European Commission, i.e. centrally authorised products (CAP), cannot be authorised nationally and vice versa.

2.1. EU marketing authorisations

The European Commission can grant authorisations *to market* medicinal products in the EEA, which are called EU marketing authorisations. They can be granted for human and veterinary medicinal products that qualify for the centralised EU authorisation procedure[1], which is compulsory for:

- all medicinal products derived from biotechnology, advanced therapy medicinal products (a medicine based or composed of on gene therapy, cell therapy or tissue engineering);
- medicine for human use containing new active substance for certain indications (e.g. cancer, diabetes, viral diseases);
- orphan medicinal products (medicines intended to treat rare diseases);
- medicinal products for veterinary use intended primarily for use as performance enhancers in order to promote the growth of treated animals or to increase yields from treated animals;

and optional for:

- other medicinal product containing a new active substance;
- other innovative medicines;
- medicines presenting interest for patients at level of the European Union;
- immunological veterinary medicinal products for the treatment of animal diseases that are subject to prophylactic measures at European Union level;
- a generic medicinal product of a CAP;
- a duplicate of a CAP and certain medicines developed for indications in children.

The applications are submitted to the European Medicines Agency (EMA) and are evaluated by its scientific committees. The EMA delivers scientific opinions upon which the European Commission bases its decisions on granting or amending EU marketing authorisation. EU marketing authorisations are valid throughout the European Union and confer the same rights and obligations in each of the Member States as marketing authorisations granted by that Member State.

Information about all medicinal products, which have been granted EU marketing authorisation, can be found in European public assessment reports (EPAR) on the EMA website http://www.ema.europa.eu. The EU legislation on medicinal products is published on the European Commission website http://ec.europa.eu/health/documents/eudralex/index_en.htm.

2.2. Authorisation by the national health authorities of the EU Member States

The national health authorities of the EEA countries may grant marketing authorisations for medicinal products other than those falling under the mandatory scope of the centralised procedure. In these cases, applications are submitted to national health authorities and the national marketing authorisations granted are valid only in their national territory.

3. Certification of medicinal products in the EU

The EU authority granting the marketing authorisation has also the responsibility to issue certificates. EU law[2] instructs the certifying authorities in the EU to comply with the arrangements of WHO[3].

3.1. Certification of medicinal products authorised by the European Commission (centrally authorised products)

The European Commission has delegated its certifying power to the EMA. The EMA can issue certificates only if the application for marketing authorisation has qualified to be assessed through the centralised EU authorisation procedure (see section 2.1). In practice this means that, if the European Commission has authorised a medicinal product, the EMA can certify it on its behalf.

This document focuses on the EMA certification scheme. More information on EMA certification is available on the EMA certificates of medicinal products web page:
https://www.ema.europa.eu/en/human-regulatory/post-authorisation/certification-medicinal-products

3.2. Certification of medicinal products for use outside the European Union (EU-M4all), previously known as Art. 58 procedure

The EU-M4all legal basis Art. 58 of Regulation (EC) No 726/2004 provided that the EMA can give a scientific opinion, in the context of cooperation with WHO, for the evaluation of certain medicinal products intended exclusively for markets outside the European Union. Such opinions are drawn up by the Committee for Medicinal Products for Human use (CHMP), following a review of the quality, safety and efficacy data, analogous to the review undertaken via the centralised procedure, after consultation with the WHO.

In case the opinion pursuant to Art. 58 has been obtained, the product can be certified using the usual EMA certification procedure.

3.3. Certification of medicinal products authorised by EU Member States (nationally authorised products)

The national health authorities of the EU Member States can issue certificates for any medicinal product whose marketing authorisation is valid in their territory. Currently the schemes within the EU Member States vary. This means that templates, conditions and terms for certification may differ from one EU Member State to another. More information about the EU national certification can be requested from each competent authority.

4. EMA arrangements for certification of medicinal products

The EMA supports the WHO efforts for global harmonisation by following closely the internationally recognised WHO certification scheme[3]. The EMA certificates are intended to support regulatory procedures for medicinal products in countries outside the EU/EEA.

4.1. Status of EU marketing authorisations

The EMA certifies the EU marketing authorisation, and the related annexes, as they are when the certificate is issued. Any variations and changes to the authorisation can be implemented on EMA certificates once the European Commission has endorsed the decision to amend the authorisation. The exceptions are:

- minor variations to the marketing authorisation (e.g. type IA, IB[4] and changes in the labelling or the package leaflet not connected with the summary of product characteristics[4]);
- any variations that do not amend the terms of the decision granting the marketing authorisation (a Commission decision is not required for these variations);
- type II variations not followed by a Commission decision within two-month (i.e. not falling under Article 23(ia)(a) of the Variation Regulation (EC) No 1234/2008);
- any recently discovered serious concerns related to the safe use of the medicinal product.

In the cases of the variations listed above, according to the legislation, the variation can be implemented from the date of issue of a positive opinion/notification, and the certificates reflect the EMA endorsed variations to the marketing authorisation and to the annexes. *Every certificate issued contains a hyperlink to the product webpage where, in case of recent concerns on safety, the public statement and the urgently revised European Public Assessment Report (EPAR) is available.*

The EMA also certifies products that have received a positive scientific opinion from the CHMP pursuant to Art. 58 of Regulation (EC) No 726/2004 (see also section 3.2) and the related annexes, as attached to the CHMP opinion and as amended by the CHMP.

4.2. Manufacturing site(s)

Following the WHO guidelines on the implementation of the WHO certification, the EMA certifies the GMP compliance of the manufacturing site(s), involved in the production of the finished product (drug product), the biological active substance(s)* and the site(s) responsible for batch release in the EEA.

4.3. GMP compliance of manufacturing sites

According to Directives 2001/83/EC and *Article 98 of the Regulation 2019/6*, the EEA competent authority shall ensure, by means of repeated inspections, and if necessary unannounced inspections, that the legal requirements governing medicinal products are complied with.

Before the certificates are issued, the EMA verifies that a GMP inspection of the manufacturing site(s) has been performed and that the inspected site(s) operate(s) in compliance with the principles of EU GMP or equivalent standards. The frequency of inspections is determined on a risk-based approach defined in the compilation of EU procedures, see: https://www.ema.europa.eu/en/about-us/who-we-are/inspections-human-medicines-pharmacovigilance-committees

The EMA certification of GMP compliance is based on these inspections. The manufacturing site(s) can be located outside the EEA. The EEA inspectorate(s) or, in case of operational mutual recognition agreements (MRA) or agreements on conformity assessment and acceptance of industrial products (ACAA) between the EU and another country, the inspectorate of the MRA or ACAA partner inspects the sites regularly.

4.4. Languages for EMA certificates

The EMA can issue certificates in *English (EN), Spanish (ES), French (FR) and/or Portuguese (PT), and in any combination thereof*. The product information is in the requested language(s) and EPARs are in English.

Certificates with annexes for products under EU-M4all are only issued in English.

4.5. Annexes to EMA certificates

The EMA attaches only certain annexes to certificates. An overview of the annexes that can be attached to certificates are listed below. Any other supplementary information required by the requesting authority should be requested directly from the applicant.

* The way in which biological products are produced, controlled and administered makes some particular precautions necessary. Unlike conventional pharmaceutical products, which are normally produced and controlled using reproducible chemical and physical techniques, biological products are manufactured by methods involving biological processes and materials, such as cultivation of cells or extraction of material from living organisms. These processes display inherent variability, so that the range and nature of by-products are variable. For this reason, in the manufacture of biological products full adherence to GMP is necessary for all production steps, beginning with those from which the active ingredient is produced (*WHO Good manufacturing Practices for biological products, WHO Technical Report Series, No. 996, 2016, Annex 3*).

	Summary of Product Characteristics (SPC) (from EMA records)	**Statement of quantitative composition** (from requester)	**EPAR** (from Internet)	**Labelling** (from EMA records)	**Package leaflet** (from EMA records)	**Manufacturer of the biological active substance** **Annex II** (from EMA records)
Certificate per presentation (marketing pack)	**M**	**O**	**O**	**O**	**O**	**O**
Certificate per pharmaceutical form (incl. all strengths of it)	**M, X**	**O**	**O**	**O, X**	**O, X**	**O**
Certificates issued in case of serious concerns on the product	**M**	**O**	**O***	**O**	**O**	**O**
Certificates issued after validation of an application but before EU marketing authorisation is granted	**N**	**O**	**N**	**N**	**N**	**N**
Certificates issued for products submitted pursuant to Art. 58 of Regulation (CE) No 726/2004 *(EU-M4all)*	**M**	**O**	**O**	**O**	**O**	**O**

M = Mandatory **X** = Only one attachment as an example **O** = Optional **N** = Not available

Certificates are issued for either single presentations or a full pharmaceutical form. When requesting a certificate for a full pharmaceutical form, annexes attached "as a relevant example" are by default the presentation of the highest strength of that pharmaceutical form. The requester can express their preference to attach the annexes of a different presentation instead. Alternatively, *it can also be requested to attach the annexes containing all the presentations of the pharmaceutical form (full SPC).* The EPAR will be attached, if requested, to the certificate(s) as it is published on the EMA website.

4.6. Permission to obtain EMA certificates

Certificates are generally but not exclusively, requested by marketing authorisation holders (MAH). In order for the EMA to issue a CMP to an applicant other than the MAH, written permission from the MAH *is* required before the application can be accepted.

The permission must originate from the MAH, be in writing or a digitally signed document and be provided to the EMA with the request for certificates. For requirements with regards to digital signatures please see *Regulation (EU) No 910/2014 on the electronic identification and trust services for electronic transactions in the internal market (eIDAS Regulation).* This permission letter must be sent to the EMA certificates team for every product requested on behalf on the MAH. It will be kept on file and the requester will be asked to declare in the application form that the last submitted permission letter, if available, remains valid. A template for a permission letter can be found on the EMA certificates of medicinal products web page https://www.ema.europa.eu/en/human-regulatory/post-authorisation/certifying-medicinal-products/requesting-certificates

In certain circumstances, the importing countries can request a copy of the CMP directly from the EMA (see section 4.7).

* *Every certificate issued for a centrally authorised product contains a hyperlink to the product webpage where, in case of recent concerns on safety, the public statement and the urgently revised European Public Assessment Report (EPAR) is available. For veterinary products the hyperlink(s) might be multiple and for the entirety of the product requested.*

4.7. Authenticity of EMA certificates

To assure the authenticity of EMA electronic certificates, each certificate is provided as an electronically signed PDF document. It contains an electronic signature fully compliant with the eIDAS Regulation (Regulation (EU) N°910/2014) that guarantees the unique link to the signatory and the full authenticity and integrity of the document.

The EMA has been informed that health authorities in some importing countries require further legalisation or authentication of the EMA certificates. The EMA supports the WHO's view on the superfluous nature of authentication processes. In case of any doubt on the authenticity of certificates issued by EMA, regulatory authorities of importing countries, MAHs or any interested party can verify their authenticity in the verification system published on EMA website. Any additional query can be addressed to the Procedures Office, Committees and Quality Assurance Department by email to certificate@ema.europa.eu.

4.8. Validity of EMA certificates

No validity or expiration date is assigned to EMA certificates of medicinal products. The certificate of medicinal product reflects the EU marketing authorisation as it is on the date the certificate is issued.

4.9. Interaction with industry

The EMA recommends that companies requesting certificates from the EMA, channel any comments or proposals for improvements on the certification to their relevant trade association(s).

4.10. Fees

A fee shall apply to each request for certificates of medicinal products. The fee is composed of two parts:

- request fee;
- a fee for each certificate set.

The fees for standard procedure, urgent procedure and withdrawal of request for certificates apply in accordance with annex III of the "Rules for the implementation of Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency and other measures" as detailed in the Explanatory note on fees payable to EMA.

4.11. Trade name of the medicinal product in the importing country

The EMA can issue certificates including the trade name of the medicinal product used in the importing country, which may differ from the name in EU. The certificate will state the trade name, as provided by the requester in addition to the trade name used in EU.

5. Definitions relevant to EMA certification

- **Certificate:** Certificate of a human medicinal product and certificate of a veterinary medicinal product. Referred by WHO as "certificate of a pharmaceutical product" (CPP). It is intended to confirm the status of marketing authorisation and compliance with the principles of EU GMP or with standards equivalent to them to support regulatory processes in importing countries.

- **EPAR:** The European public assessment report. The WHO refers to this as "summary basis of approval". It provides abstract, list of authorised presentations, authorised product information (summary of product characteristics, labelling, package leaflet) in all the official EU languages, scientific discussion, steps taken for assessment and steps taken after authorisation. The EMA publishes all EPARs on its website (see Human Medicines (EPAR) for human products and Home | UPD (europa.eu) for veterinary products).
- **Importing country:** Country receiving the certificates.
- **Pharmaceutical form:** Bulk finished product e.g. tablet, capsule, solution for injection. A pharmaceutical form of a medicinal product covers all pack types, package sizes and strengths. The WHO refers to it as "dosage form".
- **Presentation:** The final sales pack size for a given pack type, strength and pharmaceutical form of a medicinal product. A presentation of a medicinal product is identified with a unique number in the "community register of medicinal products".
- **Standard procedure:** Procedure for issuing certificates of medicinal product within 10 working days, starting on the following working day of receipt of request.
- **Urgent procedure:** Procedure for issuing certificates of medicinal product within 2 working days, starting on the following working day of receipt of request.
- **Withdrawal of request for certificates:** When a request for certificates is withdrawn by the requester following confirmation by the Agency of the start of the procedure.

6. References

1 Council Regulation (EC) No 726/2004 laying down EU procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products.

2 Directive 2001/83/EC on the EU code relating to medicinal products for human use: Article 127 and *Article 98 of the Regulation 2019/6* relating to veterinary medicinal products.

3 *WHO certification scheme* on the quality of pharmaceutical products moving in international commerce as published in the WHO Technical Report Series *1033, 2021 (*Fifty-fifth *report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations).*

4 Commission Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products.