EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Veterinary Medicines Division

Procedural advice for vaccine platform technology master file (vPTMF) certification

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1. Introduction

This document is intended to provide advice to marketing authorisation (MA) applicants and marketing authorisation holders (MAHs) on issues associated with the submission, evaluation, certification and use of a veterinary vaccine platform technology master file (vPTMF) by the European Medicines Agency (EMA). The detailed scientific requirements for an application for veterinary vPTMF certification are described in Commission Delegated Regulation (EU) 2021/805 of 8 March 2021 amending Annex II to Regulation (EU) 2019/6 of the European Parliament and of the Council and in the Guideline on data requirements for vaccine platform technology master files (vPTMF) (EMA/CVMP/IWP/286631/2021).

2. Legal framework

The principles, evaluation and certification of vPTMF are described in Section V.4 of the Commission Delegated Regulation (EU) 2021/805 of 8 March 2021 amending Annex II to Regulation (EU) 2019/6 of the European Parliament and of the Council.

3. Principles of the vPTMF certification

A vPTMF is defined as a stand-alone part of the marketing authorisation application dossier for a vaccine, which contains all relevant data relative to the platform for which there is reasonable scientific certainty that will remain unchanged regardless of the antigen(s)/gene(s) of interest added to the platform. The nature of the data to be included in the vPTMF will depend on the type of platform.

The stand-alone part may be common to one or more monovalent and/or combined vaccines presented by the same applicant or marketing authorisation holder for the same target species.

The use of the vPTMF certification system is optional. For combined vaccines, containing active substances produced using different vaccine platform technologies, as defined in V.4.1.1 of Annex II of Regulation (EU) 2019/6, the platform technology(ies) to be included in vPTMF(s) shall be specified and a separate vPTMF shall be required for each of those selected by the applicant.

It is expected that all platform technologies fulfilling the definition in Annex II of Regulation (EU) 2019/6 will be generated using biotechnological processes (recombinant technology, controlled expression of genes, etc.). Therefore, the vaccines they are included in would fall under the scope of the centralised procedure as described in Article 42(2) of Regulation (EU) 2019/6.

The vPTMF certification (1st step) consists of a centralised assessment of the vPTMF application dossier submitted by the applicant/MAH, which results in a certificate of compliance to Union legislation, issued by the EMA. This certificate is valid throughout the European Union.

As a second step, the EMA shall take into account the certification, re-certification or variation of the vPTMF for the concerned medicinal product(s) (Figure 1).

This document focusses on the first step. For the second step, changes to existing marketing authorisations resulting from vPTMF certification procedures (i.e. inclusion of a new, updated or amended vPTMF) will be introduced via variation following the relevant guidance (see References).

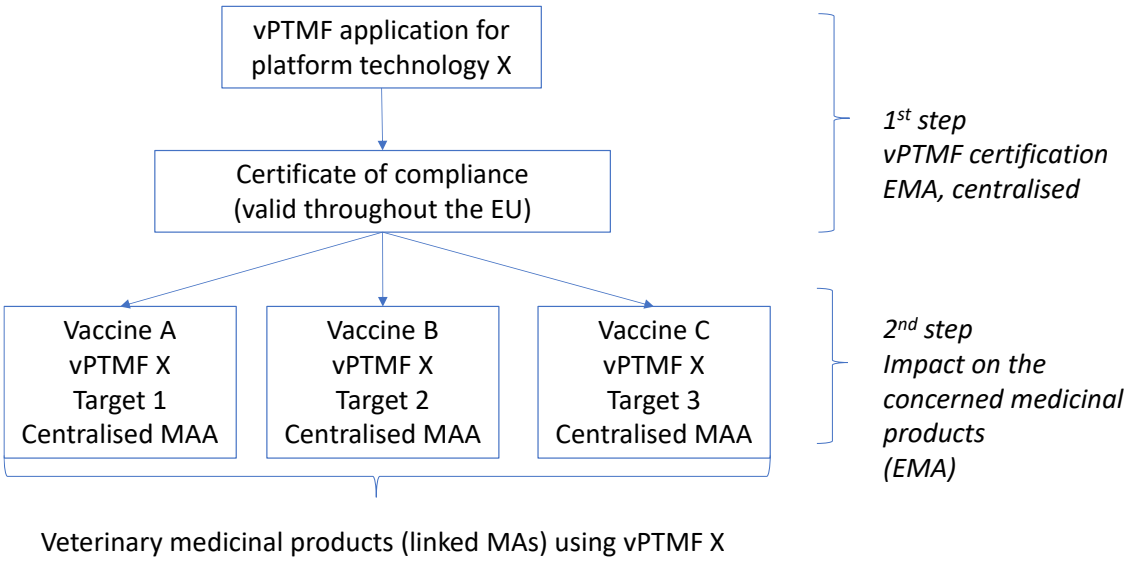


Figure 1: General principles of a vPTMF

A marketing authorisation (MA) or a marketing authorisation application (MAA) may contain one or more vPTMF certificates and respective vPTMF data.

Two different scenarios referred to as 'triggers' are possible for the initial certification of a vPTMF (see Annex 1):

- **Trigger 1:** For new vaccine platform technologies which have not been already authorised in the Union, the evaluation of vPTMF(s) will be carried out as part of the evaluation of the full marketing authorisation dossier of the vaccine in which they are included. To this end, a full marketing authorisation application dossier should be submitted to the Agency, including all the vPTMFs corresponding to each single vaccine platform technology for which the use of a vPTMF is intended. It is also possible to evaluate a vPTMF application as part of an initial marketing authorisation for a vaccine containing a platform technology already used in an authorised vaccine(s) in cases where the introduction of vPTMF(s) in the existing vaccine(s) is not envisaged.

- **Trigger 2:** For platform technologies used in currently centrally authorised vaccines, the evaluation and certification of a vPTMF will be performed through a separate procedure. In this case, an application for a vPTMF will be submitted to the Agency containing the data corresponding to the platform technology for which a vPTMF is intended.

The decision as to whether a particular vPTMF is to be used for an existing MA rests with the MAH, who may decide that even though the same platform technology is used in several MAs, the MAH only wishes to link the certificate to some, not all such MAs.

Once the applicant/MAH chooses to use the vPTMF certification system, all variations to the corresponding MAs concerning the platform technology included in an approved vPTMF will have to be submitted through the same certification system. Either the same change is made to all linked MAs or the particular MA in question is removed from the vPTMF system.

4. Initial certification of a vPTMF

4.1. Trigger 1 – New MAA for a vaccine via the centralised procedure

In the framework of a new MAA assessment via the centralised procedure for a vaccine based on a new platform technology or an existing platform technology used in centrally authorised vaccines. In this case, the certification of the vPTMF is an intrinsic part of the assessment of the MAA dossier submitted to the Agency.

4.1.1. Pre-submission activities

The MA applicant should inform the Agency that they intend to use the EU vPTMF certification system (see Annex 2). Applicants may ask for a pre-submission meeting to obtain further procedural and regulatory advice from the Agency.

4.1.1.1. Letter of intent to the Agency

For applications for vPTMFs linked to the submission of an initial MAA, the intention to use vPTMF shall be confirmed no later than 2-3 months prior to the submission of the MAA, either via notification to the Agency or via inclusion in the pre-submission request form. Information that should be provided:

- Intent to use the EU vPTMF certification system. For combined vaccines, identification of the platform technology(ies) for which the use of vPTMF is intended.

4.1.1.2. Appointment of rapporteurs

The rapporteur and co-rapporteur appointed by the CVMP for the evaluation of the MAA will also be responsible for the evaluation of the corresponding vPTMF(s). The appointment of rapporteurs will be notified to the MA applicant.

4.1.2. Submission activities

The submission dates for vPTMF(s) will follow the standard submission deadlines for MAAs published by the Agency and available on the EMA website. The final submission date will be agreed by the applicant and the Agency.

The MA applicant shall submit the application and accompanying documentation to the Agency. All submission requirements for the Agency are published on the EMA website. The vPTMF data package should arrive simultaneously with the marketing authorisation application.

The validation of the submission will be performed by the Agency and the outcome communicated to the MA applicant with the evaluation timetable. Applicants should ensure that a technically valid submission is received by the Agency before the submission deadline. Any technically invalid applications will result in non-acceptance, which may cause a delay in the start of MAA the procedure.

4.1.3. Evaluation

For vPTMF certification applications submitted within a new centralised MAA, the assessment will by definition be embedded in the centralised evaluation procedure. The timetable will follow that of the respective MAA. An evaluation report of the vPTMF will be prepared in addition to the MA evaluation report. The vPTMF certification will occur at the stage of the CVMP opinion on the MAA.

4.1.4. Certification

Within 15 working days of the adoption by the CVMP of a positive evaluation report, the Agency will issue a vPTMF certificate. The vPTMF evaluation report will accompany the certificate. At the end of the certification procedure, the certified vPTMF will effectively form part of the MA dossier of the vaccine. A variation not requiring assessment (VNRA) to add the vPTMF to the MA dossier is not needed in this case (Trigger 1).

Within 15 working days of the adoption by the CVMP of a negative evaluation report, the Agency will issue a letter refusing the grant of a certificate for a vPTMF to the applicant. The vPTMF evaluation report will be attached to the refusal letter.

4.2. Trigger 2 – New vPTMF for a vaccine platform technology used in authorised vaccine(s) via the centralised procedure

In the case of vaccine platform technologies contained in vaccines authorised via the centralised procedure, the MAH may initiate the vPTMF certification at any time.

It is encouraged that the data submitted for certification are identical to the corresponding data approved in one linked MA, and no changes are proposed during the certification. In the case of a vPTMF application for a vaccine platform technology used in different authorised vaccines where differences in the data packages exist, the MAH may consider harmonising the respective dossiers before applying for a vPTMF. Alternatively, the MAH could choose one of the MA dossiers to apply for the initial vPTMF and then consider harmonising the rest of the dossiers based on the approved vPTMF.

It is not possible to certify a vPTMF that might change during the procedure. Therefore, it is strongly advised not to initiate a vPTMF certification when there are ongoing variations related to the content of the vPTMF in the individual MA(s). Additionally, MAHs should not submit variations related to the content of the vPTMF until the vPTMF is certified.

4.2.1. Pre-submission activities

Prior to the submission of the vPTMF application, the MAH should inform the Agency that they intend to use the EU vPTMF certification system (see Annex 2). MAHs may ask for a pre-submission meeting to obtain further procedural and regulatory advice from the Agency.

4.2.1.1. Letter of intent to the Agency

MAHs should ideally inform the Agency of their intention to submit vPTMF applications approximately 2-3 months before submission, specifying the intended submission date. Information that should be provided:

- For combined vaccines, identification of the vaccine platform technology(ies) for which the use of vPTMF is intended.
- A list of MAs to which the respective vPTMF will apply.

4.2.1.2. Appointment of rapporteur(s)

For the evaluation of the vPTMF, one rapporteur and one co-rapporteur will be appointed by the CVMP. The appointment of rapporteur(s) will be notified to the MAH. The rapporteur and co-rapporteur responsible for the authorised product(s) will be appointed as rapporteurs for the evaluation of the vPTMF application.

The rapporteur(s) will be responsible for the evaluation of the vPTMF certification application on behalf of the EMA.

4.2.2. Submission and validation

The monthly deadlines for submission of applications for vPTMF certification will be published on the EMA website.

The MAH shall submit the application and accompanying documentation to the Agency. All submission requirements for the Agency are published on the EMA website.

The validation of the submission will be performed by the Agency and the outcome communicated to the MAH.

4.2.3. Evaluation

An evaluation report will be prepared by the appointed rapporteur(s) and circulated for review by the CVMP. The CVMP will then make appropriate recommendations on the outcome of the evaluation.

The timetable for vPTMF certification applications for Trigger 2 will be as follows (see Annex 3):

Day -15	Submission of vPTMF application
Day 0	Validation of the vPTMF application
Day 1	Start of the procedure
Day 45	Rapporteur's evaluation report
Day 52	Co-rapporteur's comments
Day 66	CVMP comments
Day 70	Revised rapporteur's evaluation report
Day 90	**Adoption of vPTMF certificate and evaluation report** *or* adoption of list of questions and clock stop
Day 91	Re-start after submission of responses
Day 108	Rapporteur's assessment of responses and evaluation report
Day 115	Co-rapporteur's comments
Day 119	CVMP comments
Day 129	Revised rapporteur's evaluation report
Day 150	Adoption of vPTMF certificate and evaluation report

4.2.4. Certification

Within 15 working days of the adoption of a positive evaluation report by the CVMP, the Agency will issue a vPTMF certificate. The evaluation report will accompany the certificate.

Within 15 working days of the adoption of a negative evaluation report by the CVMP, the Agency will issue a letter refusing the grant of a certificate for a vPTMF to the MAH. The evaluation report will be attached to the refusal letter.

The vPTMF certificate holder will need to introduce the vPTMF certificate in the corresponding MA(s) via the relevant variation. A variation not requiring assessment shall be submitted where the vPTMF data package is identical to the corresponding sections of the authorised marketing authorisation dossier(s) or, if changes have been made, these do not have an impact on the finished product. A variation requiring assessment shall be submitted in case of changes in the vPTMF data package that may have an impact on the finished product.

5. Data requirements for initial application for certification

The content of a vPTMF to be submitted for initial certification is briefly described in Annex II (section V.4.1.2) to Regulation (EU) 2019/6. Further guidance on technical data requirements for vPTMF is provided in the 'Guideline on data requirements for vaccine platform technology master files (vPTMF)' (EMA/CVMP/IWP/286631/2021).

6. Changes to the content of a vPTMF (Variations)

6.1. Legal framework

A variation to the terms of a vPTMF certificate must be submitted in accordance with Commission Implementing Regulation (EU) 2021/17 of 8 January 2021 establishing a list of variations not requiring assessment in accordance with Regulation (EU) 2019/6 and with the EMA/CMDv Guidance on the details of the classification of variations requiring assessment according to Article 62 of Regulation (EU) 2019/6 for veterinary medicinal products and on the documentation to be submitted pursuant to those variations (EMA/CMDv/7381/2021; see Chapter H).

6.2. Procedure for variations to the terms of a vPTMF certificate

Changes to the content of a vPTMF for a vaccine authorised in the Union shall be subject to a scientific and technical evaluation carried out by the Agency. The variation submission, data requirements and evaluation will follow the current established procedure for variations to centralised MAs.

The Certificate Holder shall submit the vPTMF variation application and accompanying documentation to the EMA. For variations requiring assessment, an expert statement including the Certificate Holder's view of the possible impact of the vPTMF to each linked MA should be provided.

In the case of a positive evaluation, the Agency shall re-issue the certificate of compliance with Union legislation for the vPTMF with the variation evaluation report attached, if applicable.

The vPTMF certificate holder will need to introduce the updated vPTMF certificate in the corresponding MA(s) via the relevant variation. The type of variation required i.e. variation not requiring assessment or variation requiring assessment, will depend on the impact of the change introduced in the vPTMF on the finished product.

7. Use of vPTMF certificates when submitting new MAAs

When submitting an application for a new MA, the applicant should notify the EMA, if appropriate, of the use of vPTMF certificates in the application.

The applicant will be required to provide to the EMA all valid vPTMF certificates of compliance to Union legislation and accompanying evaluation reports.

The list of relevant medicinal products to which the vPTMF applies should be updated by the MAH after the new MA has been granted. The MAH should have a record of the MAs to which the vPTMF applies and should provide it to competent authorities upon request.

8. References

Regulation (EU) 2019/6 of the European Parliament and the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC

Commission Delegated Regulation (EU) 2021/805 of 8 March 2021 amending Annex II to Regulation (EU) 2019/6 of the European Parliament and of the Council.

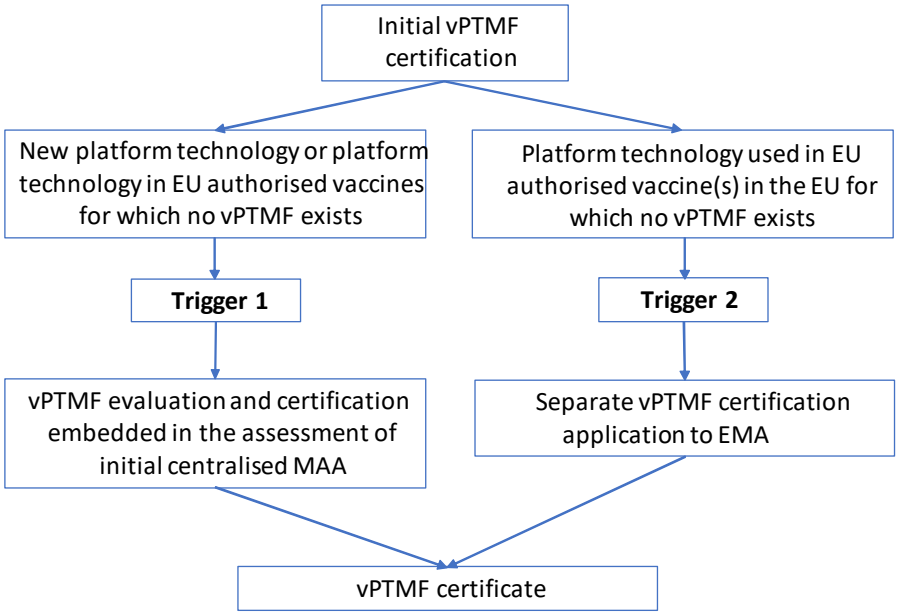
Commission Implementing Regulation (EU) 2021/17 of 8 January 2021 establishing a list of variations not requiring assessment in accordance with Regulation (EU) 2019/6 of the European Parliament and of the Council

EMA/CMDv Guidance on the details of the classification of variations requiring assessment according to Article 62 of Regulation (EU) 2019/6 for veterinary medicinal products and on the documentation to be submitted pursuant to those variations (EMA/CMDv/7381/2021)

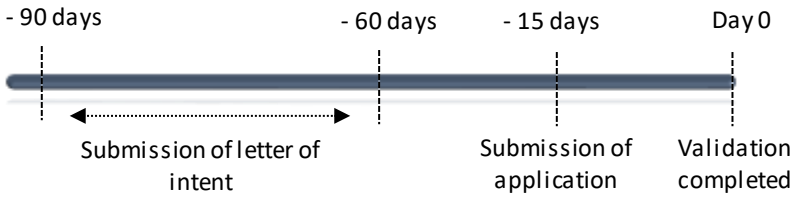
Guideline on data requirements for vaccine platform technology master files (vPTMF) (EMA/CVMP/IWP/286631/2021)

9. Annexes

Annex 1 - Triggers for vPTMF certification



Annex 2 - Pre-submission activities for initial certification of a vPTMF



Annex 3 – Timetable for certification of a vPTMF – Trigger 2