METHOD OF SUBMISSION OF THE APPLICATION AND DOCUMENTATION FOR THE VARIATION TO THE MARKETING AUTHORISATION FOR A MEDICINAL PRODUCT FOR HUMAN USE

The application for the variation to the marketing authorisation for a medicinal product (variations) shall be prepared in accordance with the Law on Medicinal Products (Official Gazette of Montenegro, No. 14/26), the Rulebook on the Conditions for Granting a Marketing Authorisation for a Medicinal Product for Human Use (Official Gazette of Montenegro, No. 22/26) (hereinafter: the Rulebook),the EC guideline "Guidelines on the details of the various categories of variations, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products and on the documentation to be submitted pursuant to those procedures" (hereinafter: the variation classification guideline), available at the following link: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ%3AC_202505045 and in accordance with these instructions.

The application for the variation to the marketing authorisation for a medicinal product shall be submitted to the registry office of the Institute for Medicines and Medical Devices (hereinafter: CInMED) or through the CInMED portal for electronic submission of documentation.
The documentation shall be submitted exclusively in electronic form, in the following formats: Word document (docx), Excel Worksheets (xlsx), and PDF, following the CTD format.
If the documentation is submitted to the CInMED registry office, the application may be submitted on each working day from 9:00 a.m. to 12:00 p.m.

In addition to the documentation submitted in electronic form, the following shall also be submitted:

- A cover letter for the notification/approval of the variation in paper form (signed and stamped by the applicant), containing the information on the medicinal products subject to the variation and a brief summary of the changes being notified. If the variation is submitted at the request of the CInMED, this shall be indicated in the cover letter;
- A completed application form for the notification/approval of a variation for a medicinal product for use in human medicine in paper form (signed and stamped by the applicant) or in electronic form signed with an electronic signature and electronic seal in accordance with the law governing electronic identification and electronic documents. The valid form available on the Institute's portal shall be used.

The following shall also be submitted together with the application for the notification/approval of the variation:

- A document (Word or PDF) containing a comparative tabular presentation of the existing and proposed data ("present/proposed"), where the changes are too extensive to be presented in detail in the application form.
- Annex 1 to the application form: Classification of variations – medicinal products for human use. This annex shall be submitted as a separate document, with mandatory indication of the conditions that need to be fulfilled, as well as the documentation that must be enclosed, depending on the type of application to which the relevant variation relates.
- Documentation on the variation in accordance with the applicable variation classification guideline, depending on the type and subtype of the variation. For Type II variations for which the

required documentation is not specified in the variation classification guideline, relevant data/documentation supporting the requested change shall be submitted;

For the correct grouping of variations upon submission of the application, it is recommended to use the guidance: *CMD(h) Examples for acceptable and not acceptable groupings for MRP/DCP products (*CMDh_173_2010_Rev24_2025_10_clean_-_Examples_for_groupings_for_MRP_DCP_MPs.pdf*),* *CMD(h) Questions & answers on variations* (Heads of Medicines Agencies: Questions & Answers) and *EMA Grouping of variations: questions and answers* (Grouping of variations: questions and answers | European Medicines Agency (EMA).

For changes in the Restricted part of the Active Substance Master File (ASMF restricted part; RP), the Restricted part shall be submitted via the link: https://secure.cinmed.me//eservis/strani-korisnik. Together with the ASMF, a Letter of Access and/or Submission Letter shall be submitted in accordance with Annex 2 or Annex 3 of the guideline *Guideline on Active Substance Master File Procedure, CHMP/QWP/227/02 Rev 4/ Corr.* Exceptionally, for medicinal products authorised through the centralised procedure in the European Union, the ASMF RP shall be submitted exclusively upon the request of the Institute.

For the purpose of more efficient processing of applications, marketing authorisation holders are kindly requested to comply with the following instructions and notes when preparing applications for variations:

- It is necessary to state the date of implementation of the change in the designated field of the application form (**Note: for Type IB and Type II variations, the planned timeline for implementation of the variation, following its approval, should be specified; if the marketing authorisation holder is unable to comply with the planned implementation timeline, it is necessary to notify CInMED accordingly, so that it may assess whether the medicinal product may be placed on the market);*
- For Type IB and II variations, the Law on Medicinal Products does not prescribe implementation deadlines, whereby the marketing authorisation holder shall implement the change within the period stated in the application form;
- For medicinal products authorised in the EU through the CP/MRP/DCP procedure (assessed under the accelerated procedure for granting a marketing authorisation in Montenegro), where available, the variation approval issued by EMA/RMS together with the variation Assessment Report shall be submitted, where applicable. If the medicinal product is not authorised in the EU, but the variation approval is available in the country of manufacture/origin of packaging, it shall be attached to the application;
- For changes resulting from the outcome of an arbitration procedure ("referral"), PSUSA, or PRAC recommendation, the report/recommendation from the said procedure shall be submitted;
- For changes relating to the updating of product information (SmPC, PIL, packaging), an updated document in Word format with the changes indicated (track changes) as well as a clean version, with changes implemented in the last document approved by the Institute, shall be submitted in accordance with the SmPC/PIL/packaging template. In the case of simultaneous submission of

multiple variations (under one or more applications), this shall be indicated in the document in the form of comments;

- For changes relating to the updating of the CEP certificate for the active substance, it is necessary to submit a document/statement containing information on the changes in the documentation that led to the updating of the CEP certificate (it is not sufficient to state only certificate numbers in the comparative presentation of existing and proposed data ("present/proposed")), as well as information on whether the update leads to changes in the finished product manufacturer's documentation on the quality of the active substance;
- If not all revisions of the CEP certificate for the active substance have been notified to the Institute, the failure to notify all revisions shall be justified;
- For variations involving changes to the packaging text of the medicinal product labelled in the Montenegrin language, where the last approved version by the Institute was the graphical representation of the packaging, a proposed packaging text shall be submitted on the form available on the Institute's portal.

Notes:

*In the case of **unforeseen variations** (changes not covered by the current guideline on the classification of variations), the applicant is required to submit a notification of the intended application for such a variation to CInMED by e-mail at varijacije@cinmed.me, together with the recommendation of the EMA and CMDh regarding the classification of the proposed change. Following the assessment of the submitted documentation, the applicant will be duly informed on the classification of the change to be submitted.

*Variations relating to:

- the addition or deletion of the EAN code
- the removal of medicinal product information from the common SmPC/PIL texts for a product whose marketing authorisation has ceased to be valid (e.g. where one of the approved pack sizes of the medicinal product has been discontinued),

should be submitted by selecting the variation type E. z) Administrative changes / other variations.