MANNER OF SUBMITTING APPLICATION AND DOCUMENTATION FOR AMENDMENT OR SUPPLEMENT TO THE MARKETING AUTHORIZATION (VARIATIONS) FOR MEDICINES FOR HUMAN USE

Marketing authorization holder shall submit to the Institute for medicines and medical devices (hereinafter: Institute) an application for amendment or supplement to the marketing authorization (variations) in the term previously scheduled via phone **+382 20 310 280.**

All documentation, except for the cover letter and application form (which are to be submitted in paper form), shall be submitted exclusively in electronic form in the following formats: *Word* documents (docx), *Excel Worksheets* (xlsx) and PDF, following the CTD format.

As the Institute, in accordance with the Article 46 of the Law, in the procedure of issuance of Marketing Authorization for a medicine does not assess whether there is a violation of intellectual or industrial property, the documentation submitted along with the application for variation shall not contain the protection designations of the medicine's name.

Application shall be filled in accordance with the Law on Medicines ("Official Gazette of Montenegro", No 80/20), the Rulebook on More Detailed Conditions for Issuance of Medicine Marketing Authorization („Official Gazette of Montenegro", No 21/16 and 55/19) and 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: guideline on the classification of variations), which is available at the following link: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52013XC0802(04).

Application for notification/approval of variation shall be accompanied by:

- Cover letter of the application for notification/approval of variation, providing the information on the medicines subject to the variation and a brief summary of the proposed changes. If the variation is submitted at the request of the Institute, which arose as an obligation after the issuance of the marketing authorization, renewal or variation, the same must be indicated in the cover letter;
- Filled application form for notification/approval of variation (application form is available on the Institute web portal);
- *Checklist* outlining compliance with the conditions for variation classification, in accordance with the guideline on the classification of variations (where applicable);
- Documentation supporting the variation according to the current guideline on the classification of variations, depending on the type and subtype of the variation. For Type II or "*unforeseen*" variations (not covered by the guideline) for which the required documentation is not specified in the guideline on the classification of variations, the relevant data/documentation that supports the requested change shall be submitted;
- *Present/proposed* document (Word or PDF) with a comparative presentation of present and proposed data, if the changes are too extensive to be detailed in the application form.

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For proper grouping of variations when submitting the application, it is recommended to use the CMD(h) guidances *Examples for acceptable and non acceptable groupings for MRP/DCP products*, CMD(h) *Questions & answers on variations*, as well as the EMA's questions and answers *Grouping of variations: questions and answers*.

For changes in the restricted part of the Active Substance Master File (ASMF RP), please send the RP of ASMF to the address of the Institute (Institute for Medicines and Medical Devices of Montenegro, Boulevard Ivana Crnojevića 64A, 81000 Podgorica, Montenegro) or via the link https://secure.cinmed.me//eservis/strani-korisnik. Along with the ASMF, it is necessary to submit the *Letter of access* and/or *Submission Letter* in accordance with the Annex 2 and Annex 3 of the *Guideline on Active Substance Master File Procedure*, CHMP/QWP/227/02 Rev 4/ Corr. Exceptionally, for medicines authorized within centralized procedure in the European Union, ASMF RP shall be submitted upon the request of the Institute only.

For efficient processing of requests, marketing authorization holders are kindly requested to adhere to the following instructions and notes when preparing variation applications:

- It is necessary to specify the variation implementation date in the designated field of the application form;
- For medicines authorized in the EU within CP/MRP/DCP procedures (considered under the accelerated procedure for issuance of marketing authorization in Montenegro), if available, please provide the variation approval issued by EMA/RMS along with the variation assessment report, where applicable. If the medicine is not authorized in the EU but a variation has already been approved in the country of manufacturer/origin of packaging, approval of the variation should also be submitted as part of the application;
- For variations resulting from the outcome of a *referral* procedure, PSUSA or PRAC recommendation, please submit the report/recommendation of the respective procedure;
- For variations that affect PI, please provide the updated document in Word format with indicated changes (*track changes*) as well as refined (*clean*) version reflecting the changes, made in the latest approved documents by the Institute, in accordance with the PI forms which are available at the Institue web portal. If multiple variations are submitted simultaneously (through one or more applications), please leave comments within the document to indicate this;
- For changes related to the updates of CEP certificates for the active substance, it is necessary to provide a document/statement specifying changes in the documentation that caused CEP update (simply listing certificate numbers as a comparative presentation of present and proposed data is insufficient). In addition, information on whether the variation affects the quality documentation of the active substance from the finished product manufacturer shall be provided.

- If all revisions of the CEP for the active substance are not notified to the Institute, it is necessary to provide justification for not notifying all revisions;
- For variations involving changes to the labelling of medicines, if the latest approved by the Institute is a mock up in Montenegrin, a revised labelling (using the form available on the Institute web portal) shall be submitted.