Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human

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CMDh/418/2020

Practical guidance of the CMDh for facilitating the handling of processes during the COVID-19 crisis

This document is prepared by CMDh in line with and in addition to the EC/EMA/HMA "**Notice to stakeholders: Questions and answers on regulatory expectations during a pandemic**". It is intended to give further explanations and practical guidance how to address, apply and implement the provisions given by this notice for MR/DCP products.

1. We have to submit a renewal application in order to meet the deadline. However, due to COVID-19 situation we are not able to prepare the complete renewal application in time. Can we submit the application later?

MAHs are requested to submit the renewal application on time. However in the situation above, in order to meet the legal deadline, it is acceptable to submit only the renewal application form (without annexes) and renewal cover letter to the RMS and CMS, stating in the cover letter that the complete dossier is delayed due to COVID-19 and will be submitted as soon as possible but at the latest within 6 months. The MAH should use the usual submission route via CESP in eCTD-format. The RMS should already include the procedure in CTS and use the annotation field to inform the CMS of the delay in the procedure due to COVID-19.

Once the complete renewal application is submitted as additional documentation via CESP in a new eCTD sequence the applicant should indicate in the cover letter that an incomplete application has been submitted previously due to COVID-19.

2. Will the Covid-19 pandemic affect the timelines for the assessment of marketing authorisation application or post-authorisation procedures?

Regulatory procedures for products considered as critical or directly linked to the COVID-19 outbreak will be prioritized and expedited, as possible.

In certain cases for other products, the RMS, in consultation with the CMSs, may decide to delay the procedure start or re-start, if this is in the interest of the applicant and/or the RMS/CMSs.

Furthermore, it is exceptionally agreed for DCP/MRP/RUP, renewal and type II variation procedures to allow a "freezing" (holding the timetable at the same procedure Day and restarting it as soon as the response is received or as soon as the RMS AR is finalised) or "rolling back" (bring the procedure back to validation phase or back to clock stop with the usual timeframe of handling responses in the clock

stop) of the procedure timetable due to unexpected and COVID-19-related capacity issues within the RMS, or when it is not possible for applicants to submit responses due to the COVID-19 pandemic. The applicant should inform the RMS timely enough of a necessary interruption of the procedure and justify that the reason for not being able to respond is related to the pandemic. "Freezing" is envisaged to be used shortly before the end of a procedure while "rolling back" might be more applicable immediately after the procedure start/restart and before Day 120.

In these cases applicant/MAH and RMS should closely communicate the necessary steps and the RMS will decide the solution considered most suitable in the specific situation.

The RMS will inform the applicant/MAH and CMS by e-mail about any changes in the time-lines. The RMS will also update CTS accordingly and use an annotation field to note how the timeline has been changed.

3. Can I include new CMS(s) to solve shortage or availability issues due to COVID-19 into an already ongoing new application procedure?

The CMDh already published the agreed possibilities in a Position Paper concerning Applicants' request of submission of multiple applications during ongoing DCPs or inclusion of new CMS or additional strength(s) in an already ongoing DCP. However, if there are further requests for inclusion of new CMS(s) going beyond this paper this should be communicated and agreed between the applicant, the RMS and the proposed new CMS.

4. In the Notice to Stakeholders there is the possibility for a specific procedure in order to quickly implement new starting materials/reagents/active substance/intermediate/finished product manufacturing/packaging sites/suppliers or control sites without having to submit a variation before implementation called Exceptional Change Management Process (ECMP). How can we make use of this procedure and whom do we have to contact?

The ECMP is only applicable for products that are crucial for the treatment of COVID-19 patients. A notification with the heading "COVID-19, ECMP" next to the procedure number (e.g. NL/H/nnnn/001) should be sent to the RMS according to the email addresses as given below in the Annex and including all the statements regarding commitments as requested in the "Notice to Stakeholders". The notification will then be evaluated by the RMS and discussed, if necessary, with the CMS, to check/confirm if the product is indeed crucial for COVID-19 patients. The RMS will then take a decision on the acceptance of this notification and send a corresponding response within 2 working days if the notification is deemed accepted or not, to the MAH with a copy to CMS via MRVE mailbox. In case there will be no response within 2 working days, the changes notified may be implemented by the MAH. The MAH must also notify the RMS and CMS within 48 hours of implementing the change for which the ECMP is used, including a summary description of the changes made. The notification should be sent to the email addresses as given below in the Annex. The MAH is furthermore obliged to inform the supervisory authorities about the outcome of the ECMP notification. At any time after the implementation the RMS may request additional documents, if necessary. The corresponding variation has to be submitted to the RMS and all CMS as soon as the crisis situation is resolved and, in any case, no later than within 6 months following the implementation of the change. In case any of the commitments as mentioned in the "Notice to stakeholders" are not fulfilled or any critical findings in respect of the quality of the product are identified the agreed ECMP will immediately cease to be valid.

For centrally authorised products, notification should be made to the EMA.

5. I would like to use the ECMP to quickly implement a new manufacturer for the active substance or finished product, but I also need to amend the active substance specifications or finished product specifications to be applied to active substance or finished product produced at the new site. Can this be covered under the ECMP?

No, the scope of the ECMP is limited to changes to starting materials/reagents/active substance/intermediate/finished product suppliers/manufacturing sites or control sites which do not require any changes to the quality controls or quality requirements foreseen in the marketing authorisation.

As per Q3.1 of the Notice to Stakeholders, if any changes to the active substance or finished product specifications or other quality controls / requirements registered in the MA are necessary, the MAH should submit a variation in accordance with Commission Regulation (EC) No 1234/2008. Such variations can be prioritized as outlined in Q8.

6. I would like a full or partial exemption to certain labelling and packaging requirements for an authorised medicinal product crucial for COVID-19 patients in order to avoid a shortage. What can I do?

For products used in hospitals during the crisis, the CMDh agreed to flexible handling of such cases. The MAH should send an email to the relevant national competent authorities (see email addresses in the annex) with the subject title "COVID-19" next to the national product number in the email heading. Member states might have a different approach in the handling of these requests and decision will be taken on a national basis only. The specific handling for each member state has to be considered (see link to guidance provided in the annex).

7. I would like to add CMS for a product that is crucial for the treatment of COVID-19 patients to my national marketing authorisation/MRP/DCP in an expedited way. How should I communicate that?

The CMDh has agreed to perform expedited MRP or RUP procedures via a fast-track timetable (shortened TT) or even in a 0-Day procedure (approved after validation). The choice of the procedure depends on the criticality of the product as well as the decision of the RMS and the proposed new CMS. In the first instance the MAH should liaise with the proposed CMS in order to agree on their acceptance for an expedited procedure. The MAH should confirm that the product is ready to be marketed immediately after receipt of the MA. After agreement of the CMS the MAH should contact the RMS and request the MRP/RUP via a fast-track timetable or 0-Day procedure. In both cases the CMS has to agree on the procedure timetable depending on the available data. In order to assure sufficient supply of crucial medicinal products it is exceptionally acceptable to waive necessary legal updates before the MRP/RUP by giving a commitment to submit these via variation within 3 months after the end of procedure. Details have to be discussed case by case with the RMS and CMS. All requests for such expedited procedures should be addressed to the RMS and CMS by email notification with the subject "COVID-19 expedited MRP/RUP" next to the procedure number using the email addresses as given in the Annex. Furthermore, all agreements between MAH and MS in communication beforehand should be summarized clearly in the cover letter of the application.

8. I have to submit/pending urgent variation procedures for medicinal products that are crucial for the treatment of COVID-19 patients. Is it possible to expedite these variations?

According to the Regulation 1234/2008/EC and the CMDh Best Practice Guide for Variations it is generally possible to speed up variations if necessary. In case of changes different from those considered under the EC Q/A No. 3 the MAH should contact the RMS in case of such requests by sending an email notification to the RMS with the subject "COVID-19 – shortened variation TT" next to the variation procedure number. In this notification it should be sufficiently described why the TT needs to be shortened. The request will be evaluated by the RMS in consultation with the CMS promptly, at the latest within 4 working days. If there is an agreement before the submission of the variation this should be summarized in the cover letter and also stated in the section "background/scope" as "accelerated timetable". A shortening of the timetable is only possible for type IB and type II variations as type IA variations are anyway implemented before they are notified. The timetable will be agreed by RMS and CMS on a case by case basis dependent on the urgency of the matter, for example for type II variations this may also be shorter than the 30-day timetable.

9. If there are urgent variations concerning COVID-19-relevant medicinal products, would it be possible to handle the grouping possibilities in a more flexible way?

Yes, a more flexible handling of the grouping activities is possible in this specific situation. It should be discussed with the RMS before submission.

10. Is it acceptable to waive the need for a QP statement for variations/new application for a certain period if MAH/QP can prove GMP conditions (e.g. via valid GMP certificate in the EudraGMDP database etc.)?

This is not acceptable. A QP declaration is always needed but can – under circumstances – be accepted on the basis of a desktop audit.

11. Would the authorities accept a QP declaration based on a desktop audit instead of an on-site audit with a commitment to conduct the on-site audit as soon as the COVID-19 situation has improved?

This is acceptable on a case by case basis. Reference is made to the QP declaration guidance at https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guidance-template-qualified-persons-declaration-concerning-good-manufacturing-practice-gmp_en.pdf and the "Guidance on good manufacturing practice and good distribution practice: Questions and answers" published by the GMDP IWG. However, the applicant has to confirm that the on-site audit will be performed at the latest within 6 months after the pandemic has ended.

12. In case a medicinal product needed for the treatment of COVID-19 patients would be needed in the EU but would not be available, is it possible to apply for an MRP based on a third country MA?

No, it is not possible to apply for such an MRP based on a third country MA. However, it is possible to import such products. The prerequisites for import should be discussed with the relevant national authorities beforehand.

13. In case a medicinal product needed for the treatment of COVID-19 patients would be needed in the EU and a generic company had such a product and would like to apply for an expedited procedure. However, a suitable reference medicinal product (RefMP) would not be available in the EU, is it possible to apply for 10(1) application with a RefMP approved in a third country?

No, such a generic application with a RefMP in a third country would not be validated in the EU. However, it is possible to import such products. The prerequisites for import should be discussed with the relevant national authorities beforehand.

Annex: Member States' email addresses and links to published guidance

MS	Email address	Published guidance to be considered
AT	nat@basg.gv.at	https://www.basg.gv.at/en/companies/marketing-authorisation-life-cycle
BE	prelicensing@fagg.be (for new/ongoing MRP/DCP applications) postlicensing@fagg-afmps.be (for variations/renewals)	
BG		
CY		
CZ	registrace.LP@sukl.cz	
DE - BfArM	COVID-CMDh@bfarm.de	https://www.bfarm.de/DE/Service/Presse/Themendossiers/Coronavirus/_node.html;jsessionid=863A615F7B789FE87764BD1FCA5013CE.1_cid323
DE-PEI	eu-cooperation@pei.de	
DK	licensing@dkma.dk	Guidance for labelling exemptions: https://laegemiddelstyrelsen.dk/en/licensing/licensing-of-medicines/spcs,-package-leaflets-and-labelling/guidance-on-exemption-from-the-danish-executive-order-on-labelling-pursuant-to-section-38/
EE		
EL		
ES	dgestion@aemps.es	
FI	mrp@fimea.fi	
FR	Ueurop@ansm.sante.fr	
HR	interventniuvoz@halmed.HR	
HU	mrp-dcp-new-rms@ogyei.gov.hu	https://ogyei.gov.hu/
IE		
IS	ima@ima.is	
IT		
LT		
LU		
LV	variations_mrp-dcp@zva.gov.lv (MR/DC procedures NP_PI@zva.gov.lv (NP procedures)	
MT	mrp-dcp.adm@gov.mt	
NL	For requests for ECMP-COVID-19: _Dienstpostbuscmdh@cbg-meb.nl For labelling exemptions: meldpunt@igj.nl	Guidance for labelling exemptions: https://english.igj.nl/medicines/distribution-gdp/notification-of-an-interruption-on-the-market-or-a-shortage

MS	Email address	Published guidance to be considered
NO	ECMP@noma.no	https://legemiddelverket.no/andre-temaer/covid-19-og-legemidler
PL	regulatoryCOVID@urpl.gov.pl	http://www.urpl.gov.pl/pl; https://www.gov.pl/web/zdrowie/sprowadzac-leki-z-zagranicy-import-docelowy-
PT	rms.procedures@infarmed.pt (PT RMS procedures) submissao.alteracoes@infarmed.pt (national and PT CMS procedures)	
RO		
SE	ric@mpa.se	
SI		
SK	regcovid19@sukl.sk	
UK		