

~~June 2019~~ July 2022  
CMDh/401/2019, Rev. 1

## Validation of MR/Repeat use/DC procedures

### Procedural advice

All days mentioned in this document should be regarded as calendar days.

This procedure has been agreed by the CMDh to ensure that validation times are within those agreed in the Best Practice Guide for the Decentralised and Mutual Recognition Procedures (<http://www.hma.eu/91.html>).

Completion of CTS records by all MSs involved is essential for the operation of this procedure.

The validation period is 14 days and starts when the RMS and all CMSs have received a technically valid application (for DC procedures) or both the application and the AR (for MRP and RUP). It is the duty of all MSs to follow these timelines and not prolong the validation period.

If the RMS is informed by a CMS that the application is not technically valid, the RMS will adjust the validation period and inform all CMS about the new date of start of the validation phase once this CMS has confirmed receipt of a technically valid application.

The applicant should inform the RMS swiftly, at the latest within 3 days about the date of receipt of the application by the CMS. The RMS will update the CTS record accordingly (Last dossier submission) and promptly inform CMS via email about the start of the validation period and the proposed start date according to the agreed template (available in EudraPortal).

The RMS should update the CTS record with the date the assessment report (AR) was sent for MRP and Repeat-Use procedures (RUP).

The CMS should indicate and state a valid reason in CTS that the application is invalid when there are justified reasons to do so. It is not acceptable to only state in the CTS e.g. *Validation is pending*, as this would not hinder start of the procedure. An application will not automatically be set invalid if a CMS has not yet received the dossier and the validation period has not started.

The RMS may start the procedure in accordance with the proposed start date unless informed by a CMS that the application is not valid.

If a CMS sends validation comments after the validation period of 14 days, this will not delay the start of the procedure. The RMS may start the procedure as soon as all CMS who sent validation comments

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**within** the validation period have validated the application. The RMS is not allowed to backdate the start of the procedure.

If a CMS has previously informed the RMS that the application is not valid, the procedure will not be started until that CMS confirms with the RMS that the issue has been resolved and the application is valid. The CMS has a duty to update the CTS record accordingly.

The CMS must inform the RMS whether the application has become valid or is still invalid (stating the reasons) as soon as possible but at the latest within 7 days of the missing information being supplied.

If it is not expected that the application will become valid within an acceptable time, the applicant will be advised to withdraw the application in the CMS.

For validation, Member States will use the separate checklists that have been developed (<http://www.hma.eu/91.html>). In MRP/RUP, only the CMS validates the application as the product is already authorised in the RMS. For DCP, the validation check is split between RMS (full validation check) and CMS (limited list). Both CMS and RMS will start validating in parallel. The RMS will circulate the RMS checklist to the applicant and CMS via email and also add it in CTS, even if there are no outstanding issues. In all procedures, CMS should inform both the applicant and the RMS via email about any validation issues by using the respective CMS checklist. The list should also be added to CTS. However, if a CMS has no validation comments, it is sufficient to indicate this in CTS. CMS validation comments are limited to the points agreed in the checklists.

In case of an MA application with reference to a European reference product (ERP) not authorised in the RMS, the RMS requests the minimum of information on ERP on its own initiative from the MS in which the ERP is or has been authorised, in accordance with Information to be submitted by the MS of the ERP (<http://www.hma.eu/211.html>). The MS shall transmit this information within a period of one month. As soon as the ERP information is received by the RMS, it is to be circulated to the CMS and entered into the CTS database. The ERP information as defined in the legislation is deemed to be necessary for the start of the procedure and the RMS will not be able to start the procedure until this information has been provided.

## **Member state agreement upon conditions under which the RMS can start the MRP/DCP**

Applicants are advised to check the CMDh Best Practice Guide on the compilation of the dossier for new applications submitted in Mutual Recognition and Decentralised Procedures (<http://www.hma.eu/91.html>) before submission.

As many of the common validation issues are minor and not critical for starting a procedure it has been agreed to streamline the 14 day validation period by dividing the raised issues into validation issues and non-validation issues. The validation issues have to be solved during the validation period while the non-validation issues, which should not hold up the start of a procedure, will be handled in a structured manner during the procedure.

### **Validation issues – No procedure start**

*A MS can only invalidate and **prevent start of the procedure** if one of the following conditions is not met:*

- The reference product has not been licensed in accordance with the Community acquis;
- Data exclusivity period not expired;

- The chosen legal basis does not fulfil the criteria according to the current legislation;
- Application not received;
- Modules/annexes are missing or absence not justified (eq. Consultation with Target Patient Groups, Summary of Pharmacovigilance System, Environmental Risk Assessment, Specific Requirements for Different Application Types, Product information (SPC, PL, Labelling), Paediatric Regulation (where applicable), Information relating to Orphan Market Exclusivity, i.e. orphan similarity report/derogation report (where applicable) or GMP certificates and QP declarations for MRP/RUP).
- If parts of or the complete dossier are not in English, or translations e.g. M2 documents or GMP Certificates;
- The RMS is awaiting the necessary minimum information on the European Reference Medicinal Product (Where applicable);
- The CMS has not received the RMS AR (for MRP/RUP procedures);
- Application form/cover letter not signed/not signed with original signature;
- Missing/incorrect fee;
- Certain information in the application form is incorrect (e.g. information missing, incorrect type of procedure, legal basis incorrect, incorrect reference medicinal product);
- Proposed MAH not established in the EEA;
- Proposed batch releaser is situated outside the EEA;
- ASMF and/or letter of access to ASMF missing or incorrect version of the ASMF has been submitted;
- The comparator for the bioequivalence/therapeutic equivalence study does not originate from the EEA;
- The comparator for the bioequivalence study is not part of the global MA;
- The submitted documentation cannot be identified (name of applicant, name of the product etc. are missing);
- Format, media or number of copies are not acceptable/missing, insufficient number of copies submitted (cf. CMDh/085/2008 'Requirements on Submissions (number and format) for New MA Applications within MRP, DCP and National Procedures');
- Specific published national requirements are not met cf. Table "Data requested for New Applications in the MRP/DCP..."(<http://www.hma.eu/91.html>);

#### **Non-validation issues– RMS empowerment to start the procedure**

*The RMS can start the procedure although the following issues still haven't been solved on Day 0. The applicant still has the duty to rectify the missing/incorrect documents by Day 10 for MRP/RUP or Day **50-30** for DCP, at the latest. If the applicant fails to submit in due time, the MS will bring the matter to the RMS and/or to the applicant in the next RMS AR or date for CMS comments.*

- In case a CMS sends validation comments that go beyond the points agreed in the CMS checklists;
- If **Non published** Additional national data is requested. Beyond **published** Table "Data requested for New Application in the MRP/DCP which are not stated in the current EU legislation and/or in Volume 2B, Presentation and format of the dossier Common Technical Document (CTD) and/or in the EEA approved guidelines/Recommendation papers"(Doc. Ref. CMDh/043/2007)".

- A MS states in the CTS Validation pending without given any reason;
- The CMS has not notified the RMS within the foreseen automatic validation period;
- If the CMS start the evaluation and raise scientific evaluation issues such as labelling of the medicinal product, questioning the applicants submitted justification for a biowaiver, the submitted justification for absence of readability test, requests for missing or updated QP declarations or manufacturers authorization/GMP Certificate as the submitted is expired/close to expire.
- The applicants proposed dispensing/classification cf. Section 2.3 in the Application Form (Rx/OTC).The applicant shall though be aware of that accepting the application as valid not necessarily is an acceptance of the proposed classification of the medicinal product. The applicant should therefore very carefully consider whether or not the dossier fulfils/is in accordance with the MSs practise on classification.
- Mock-ups (may be fulfilled during the assessment period);
- Specimen (samples of API and/or medicinal product) or a declaration that they will be sent are missing (may be fulfilled during the assessment period);
- The name of product stated in the Application Form and the Cover Letter should be the same (strongly recommended cf. CMDh Cover Letter Template but not a validation issue);
- Module 1.3.5 Product Information already approved in the Member States (as only in national language);
- Module 1.3.6 Braille certificate is missing;
- Original signature of Experts in Module 1.4 (may be fulfilled during the assessment period);
- Table of Content in Module 2.1 is missing;
- The Introduction in Module 2.2 is missing;
- If the CMS raise **post procedure issues/commitments concerning the details in the national phase** (e.g. discussion of naming of the product<sup>1</sup> , Braille declaration, legal status of the product, request for signed national translations of SmPC, PL and labelling, signed declaration of intended pack sizes and pack types to be marketed.

*It should be noted that these are only examples of non-validation issues. The list is not exhaustive and may be extended on an on-going basis.*

The RMS/CMS should clearly state during the validation phase if a raised issue is considered a 'validation issue' or a 'non-validation issue'. This is clearly reflected in the validation checklists named above (<http://www.hma.eu/91.html>).

Should the RMS be in doubt whether an item is raised as validation issue or non-validation issue it is strongly recommended that the RMS liaise with the MS concerned before starting the procedure.

In exceptional cases, if an agreement between the RMS and the CMS cannot be reached both parties are encouraged to bring the issue to discussion at the CMDh meeting.

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<sup>1</sup> The Name of a generic product referring to a Centralised approved product has to be agreed at finalisation of the procedure