MARKETING AUTHORIZATION PROCEDURES IN THE EUROPEAN UNION – MAKING THE RIGHT CHOICE

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INTRODUCTION

The European Union, consisting of 27 Member States, has continuously worked on improving and streamlining drug review and marketing authorization processes. There are currently three different procedures that can be used to submit a medicinal product for marketing approval in the European Union. This paper will briefly outline the available avenues and describe when one might be used over another.

The three described procedures are published by the European Commission in consultation with the competent authorities of the Member States, the European Medicines Agency (EMEA), and interested parties. The three procedures that are currently applicable are:

- Mutual Recognition Procedure (MRP)
- Decentralized Procedure (DCP)
- Centralized Procedure (CP)

In each case, the legal basis for a marketing authorization application may vary from a full application and submission of all data regarding the pharmaceutical, pre-clinical and clinical trials, to bibliographic or a well-established medicinal use application, or another basis, such as a generic application. It is also important to note that the marketing authorization process is dynamic and the underlying dossier must be regularly updated to ensure that scientific progress and new regulatory requirements are respected.

WHICH PROCEDURE IS APPLICABLE?

While there are three different procedures, each one is not applicable in every case. There are specific times when it is mandatory to use the Centralized Procedure (CP). Orphan medicinal products and medicinal products, which contain new active substances with specific therapeutic indications, for example acquired immune deficiency syndrome (AIDS), diabetes or cancer, fall within the mandatory scopes of the Centralized Procedure. Other mandatory scopes include biotechnology-derived medicinal products and advanced therapy medicinal products. Optional scopes include medicinal products with significant therapeutic, scientific or technical innovation.

When a medicinal product does not fall within the mandatory scopes of the CP, the applicant may apply for marketing authorization in one or several countries in the European Union by using the Mutual Recognition Procedure (MRP) or the Decentralized Procedure (DCP), in which case the competent authorities of the Member States are responsible for granting the authorizations. At the end of a successful procedure, the medicinal product receives one or several national marketing authorizations in the selected countries. In both the MRP and the DCP, the applicant should request one Member State to act as Reference Member State (RMS). It is the RMS that prepares an Assessment Report on the medicinal product and sends to the other Concerned Member State(s) (CMS/s) where the applicant would like marketing authorization in. Independent national procedures are strictly limited to the initial phase of the MRP and granting of the marketing authorization by the RMS.

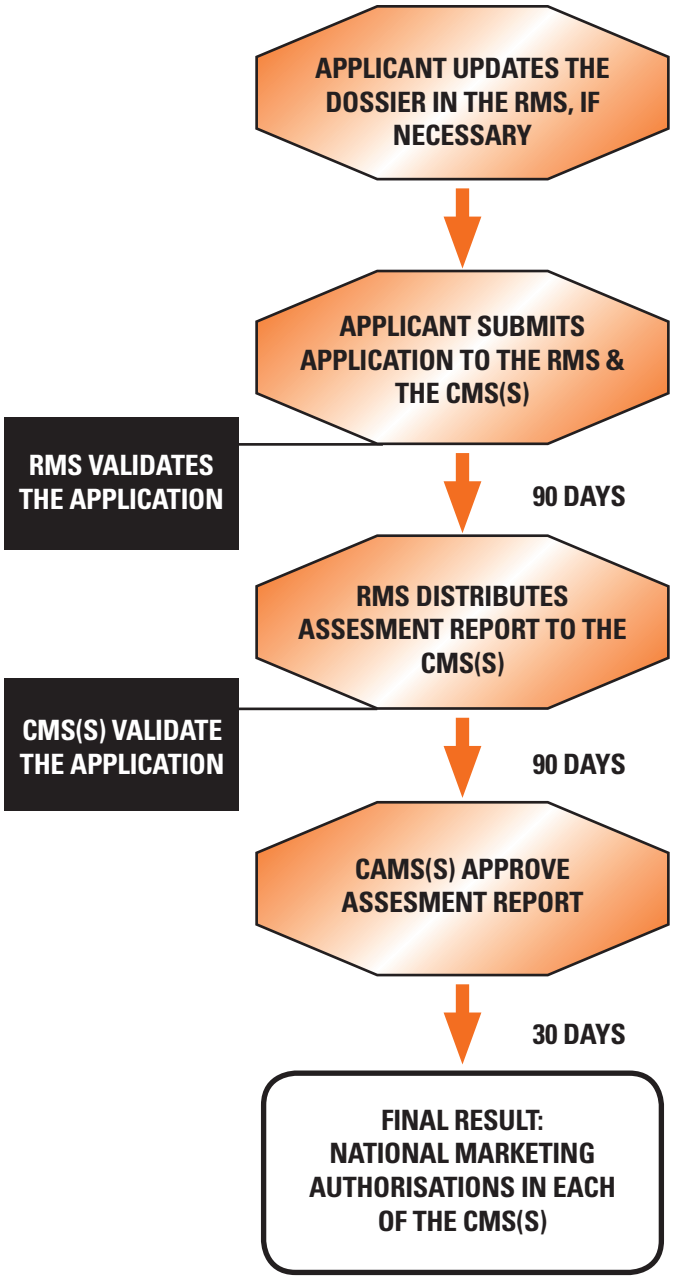
MUTUAL RECOGNITION PROCEDURE (MRP)

The MRP has been in place in the EU since 1995. The objective of this procedure is to obtain marketing authorizations in one or several Member States, when the medicinal product has already been granted authorization by at least one country in the European Community. In this case, the applicant requests one or more CMS(s) to mutually recognize the authorization granted by the RMS. If the marketing authorization in the RMS is based on an old dossier format, it is an obligation to reformat the dossiers before starting the MRP.

The marketing authorization holder should submit an application to the competent authorities of the RMS and each of the CMS(s). Within 90 days of receipt of a valid application by the RMS, the RMS provides the Assessment Report, or if necessary, updates any existing one and sends it together with other documents to the CMS(s) and to the applicant. The RMS launches the clock after receipt of the Assessment Report and validation of the application by each of the CMS(s). Within 90 days, the CMS(s) recognize the decision of the RMS. Thirty days after the close of the procedure, the competent authorities of the CMS(s) adopt a decision and grant marketing authorization. Therefore, at the end of the MRP with a positive agreement, a national marketing authorization will be issued in each of the CMS(s).

FIGURE 1: MUTUAL RECOGNITION PROCEDURE

Marketing approval already granted by an EU Member State, now referred to as the Reference Member State (RMS)

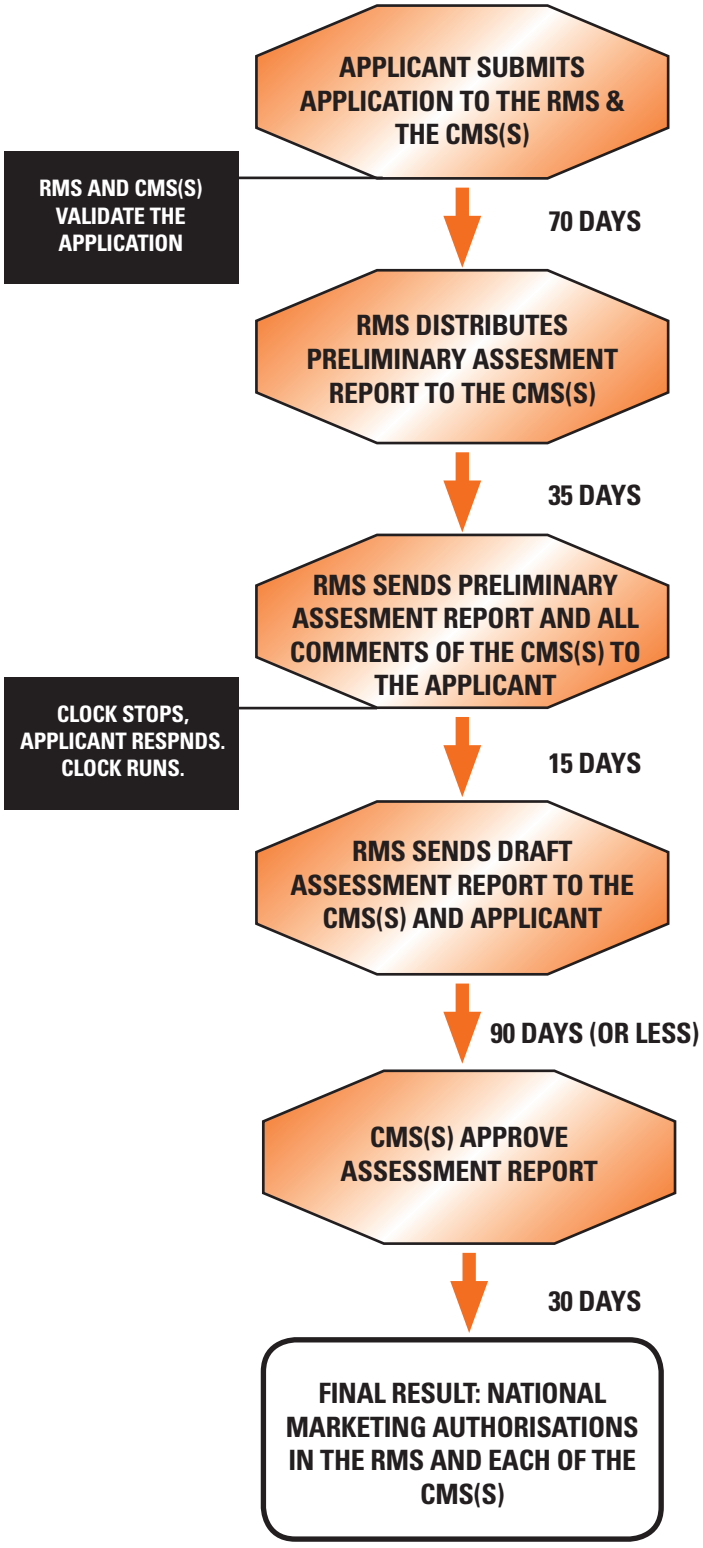


DECENTRALIZED PROCEDURE (DCP)

The new DCP came into effect in the EU in 2005. The objective of this procedure is to obtain marketing authorizations in several Member States, when no marketing authorization has been granted in the European Community. The applicant should send an application to the competent authorities of each of the Member States, where there is intent to obtain a marketing authorization. The applicant may designate a country to act as the Reference Member State (RMS). Selection of the RMS depends on many considerations including workload, previous experience, interests, and acceptance of the dossier by the RMS.

The RMS will start the procedure after the application is determined to be complete by both the RMS and all the CMS(s). The RMS forwards a preliminary Assessment Report on the dossier to the CMS(s) and the applicant within 70 days. The CMS(s) is asked to give comments on the proposed national prescription status and to inform the RMS. On day 105, the RMS will forward all comments to the applicant and stops the clock if necessary, until the applicant prepares a response document. The RMS prepares a Draft Assessment Report on day 120 and may close the procedure if a consensus has been reached between the CMS(s) and the RMS. Otherwise, the CMS(s) has 90 more days to approve the Draft Assessment Report, and other documents. Competent authorities of the RMS and the CMS(s) adopt a decision within 30 days after acknowledgement of their agreement to the Assessment Report and other documents. At the end of the Decentralized Procedure with a positive agreement, a national marketing authorization will be issued in the RMS and each of the CMS(s).

FIGURE 2: DECENTRALIZED PROCEEDURE



WHEN THE MEMBER STATES DISAGREE

Where one or more Member States cannot recognize an authorization already granted in an MRP or a final assessment and product information prepared in a DCP, the disagreement is referred to the Coordination Group for Mutual Recognition and Decentralized Procedure for Human Medicinal Products (CMDh). If the Member States still fail to reach an agreement within the CMDh, the matter is referred to the Committee for Medicinal Products for Human Use (CHMP) in the EMEA for arbitration, where there is a detailed reasoning for the disagreement. This referral is automatic and mandatory, once a Member State has raised a concern on the grounds of potential serious risk to public health. In this case, when the referral procedure has been triggered, it can only be stopped if the applicant withdraws the concerned application(s)/ authorization(s) from all European Economic Area markets.

CENTRALIZED PROCEDURE (CP)

The Centralized Procedure came into being in the EU in 1995. As mentioned previously, following the Centralized Procedure is mandatory when requesting authorization for certain medicinal products.

In the Centralized Procedure, the applicant applies to the EMEA for marketing authorization and finally receives one European approval, which is valid in all 27 countries in the community, as well as Norway, Iceland and Liechtenstein. At least seven months before submission, the applicant should notify the EMEA of their intention to submit an application. Applicants have the opportunity to meet the EMEA in a pre-submission meeting, to discuss any procedural or regulatory issues. The applicant's request for eligibility for evaluation via the Centralized Procedure, together with a justification and other documents is presented to all CHMP members. Following discussion at CHMP, the EMEA informs the applicant of the CHMP position, whether the medicinal product is eligible for evaluation via the Centralized Procedure.

For any scientific evaluation, a Rapporteur, and if relevant, a Co-Rapporteur, is appointed from amongst the members of the CHMP. The role of the Rapporteur is to perform the scientific evaluation and to prepare an Assessment Report for the CHMP according to the timetable approved for the evaluation procedure. Where appropriate, the Rapporteur can be supported by a Co-Rapporteur who prepares a separate full Assessment Report or a critique of the Rapporteur's report at the discretion of the CHMP.

Once the application is validated as complete and the Rapporteur and Co-Rapporteur have confirmed that they have received the dossier, the EMEA starts the procedure at the monthly starting date published on the EMEA website. The Rapporteur/Co-Rapporteur's initial Assessment Reports are provided to the CHMP members and EMEA on Day 80. The CHMP members are assigned to conduct a peer review of the Rapporteur/ Co-Rapporteur's scientific evaluation, as well as the validity of the scientific/ regulatory conclusions reached. The adoption of the CHMP List of Questions, as well as the overall conclusions and review of the scientific data, is sent on Day 120 to the applicant. The EMEA stops the clock in order to allow the applicant time to prepare a response document. After receipt of the responses from the applicant, the CHMP adopts a timetable for the evaluation of the responses. The EMEA ensures that the opinion of the CHMP is given in 90 additional days. After the adoption of a CHMP positive opinion, the applicant provides the EMEA with final translations of the necessary documents in all EU languages including Norwegian. Finally, within 30 days the EMEA transmits the CHMP opinion and other required documents to the European Commission, and the Members of the Standing Committee, and to Norway and Iceland. The marketing authorization is granted by the European Commission and is valid throughout the Community and confers the same rights and obligations in each of the Member States as a marketing authorization granted nationally. The European Public Assessment Report (EPAR) will be published on the EMEA website, once the Commission decision has been issued.

CONCLUSION

Deciding on a suitable regulatory strategy plays an important role in gaining time on the marketing authorization of a medicinal product in the European Union. SGS Life Science Services has more than 20 years experience in marketing authorization in Europe and can help you to select the best marketing authorization strategy and follow the marketing authorization application.

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