HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide to
Renewal of Marketing Authorisations – Human Medicines

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This guide does not purport to be an interpretation of law and/or regulations and is for guidance purposes only.

1 INTRODUCTION

Applications must be submitted at least nine months before the expiry of the current authorisation, in accordance with Article 24 of Directive 2001/83/EC as amended by Directive 2010/84/EC.

An application for renewal of a marketing authorisation (MA), irrespective of whether the product is authorised nationally or through mutual recognition (MR), must be made using the EU application form for renewal of a marketing authorisation, available from the website of the EU Commission.

For MR products for which Ireland is the Reference Member State (RMS), the common renewal date will be fixed no later than the date of expiry of the Irish MA. Applications for an MR renewal procedure at a date beyond the expiry of the Irish MA will generally not be accepted.

Requests to bring forward a renewal date for one or more products in order to synchronise the renewal dates for a range of product strengths are generally facilitated. Any such proposal should be agreed with the HPRA in advance of the proposed date and requests should be directed to HPRA Receipts and Validation (submissions@hpra.ie) in the first instance.

2 STANDARD RENEWAL PROCEDURES

Products authorised nationally or through mutual recognition generally follow a 30-day standard renewal procedure timetable for all legal basis of approval. For exceptions to this rule, see section 'expanded renewal procedure with full documentation' of the CMDh Best Practice Guide on the Processing of Renewals in the Mutual Recognition and Decentralised Procedures (CMDh BPG on renewals).

For a standard 30-day renewal procedure, the applicant submits a cover letter following the CMDh template format and an EU application form (without annexes) with a declaration that full documentation will be available for submission upon request.

Changes to MA particulars will not be accepted during the standard renewal procedure. Please see relevant sections of the CMDh BPG on renewals.

3 EXPANDED RENEWAL PROCEDURES AND SUPPORTING DOCUMENTATION REQUIREMENTS

Under certain circumstances as set out in section 'expanded renewal procedure with full documentation' of the CMDh BPG on renewals, where concerns regarding the benefit/risk balance of the medicinal product have been identified, a 90-day expanded timetable with requirements for submission of the documentation listed in Annex 3 - renewal documentation of the BPG may be deemed appropriate.

The expanded timetable may be deemed appropriate irrespective of whether the product is authorised nationally or through mutual recognition. The following guidance in this section is additional to that given in the CMDh BPG on renewals.

3.1 Product Information

MA holders should update the product information (Summary of Product Characteristics (SmPC), labelling and package leaflet) as necessary throughout the life of the product. If during assessment it is identified that substantial updates are required, the product information should be updated through the appropriate variation procedure after the conclusion of the renewal.

The introduction of minor changes may be accepted during an expanded renewal procedure.

If no changes to the product information are proposed, a clean version of the latest product information should be submitted.

If changes are proposed to the product information, an annotated version of the product information should be submitted, with all proposed changes highlighted.

3.2 Addendum to the clinical overview

An addendum to the clinical overview must be submitted with all expanded renewal applications. The addendum must consist of a critical discussion addressing the current benefit/risk balance for the product, on the basis of the consolidated safety and efficacy data accumulated since the granting of the initial MA or the last renewal. This should take into account suspected adverse reaction reports, additional pharmacovigilance activities and the effectiveness of risk minimisation measures contained in the risk management plan (RMP). It must also make reference to any relevant new information in the public domain, such as literature references, clinical trials and new treatments available, which may change the benefit/risk evaluation made at the time of the original authorisation or last renewal.

The addendum must be signed by and accompanied by the CV of the clinical expert. A clear conclusive statement that the product can safely be reviewed at the end of the 5-year period for an unlimited period or any action recommended such as a further renewal in five years time is also required from the clinical expert. Refer to the CMDh BPG on renewals on the CMDh website. Marketing authorisation holders (MAHs) are also advised to consider the GVP Module VII on PSURs as guidance for the preparation of the above sections of the clinical overview.

3.3 Risk management plan (RMP)

For products with an existing RMP, the MAH must submit either:

a. an update of the approved RMP based on reassessment of the overall benefit/risk balance of the product and analysis of any additional data since the last approved RMP.

or

b. a declaration justifying why no amendments are required to the last approved RMP along with confirmation that the current approved RMP remains unchanged and applicable. This confirmation should be provided in the addendum to the clinical overview (module 2.5).

A new RMP may also be submitted as part of the renewal application where relevant.

The format and content of the RMP should follow the requirements set out in Commission Implementing Regulation on the performance of pharmacovigilance activities provided for in regulation (EC) No 726/2004 and Directive 2001/83/EC of the European Parliament and of the Council. Further guidance is provided in Module V of the Guideline on Good Pharmacovigilance Practices.

For products without an existing RMP, this should be indicated in module 1.8.2.

Reference to submission or non-submission of an RMP should be included in the covering letter to the HPRA. A brief justification of the reasons for non-submission must be provided where relevant.

3.4 Manufacturers

For sites within the EEA, current manufacturing authorisations or certificates of GMP compliance should be provided for the manufacturer(s) of the medicinal product listed in the application form. A reference to the Community EudraGMDP database, if available, will suffice.

For sites outside the EEA, documentary evidence issued by an EEA competent authority or MRA partner authority indicating the date, inspection team and outcome of the most recent inspection at the site is required.

Declarations are required in relation to the GMP status of the active substance(s). For more details, please refer to the EU renewal application form.

PA holders are asked to ensure that the manufacturers of the active substance and finished product listed in the application form are those approved by the HPRA. Any change in manufacturers must be done by variation before submission of the renewal.

3.5 Quality overview

The quality overview must be signed and accompanied by the CV of the expert. It should include a declaration of compliance with Article 23 of Directive 2001/83/EC, as amended, which obliges MA holders to '...take account of technical and scientific progress and introduce any changes...'. The statement should confirm that all changes relating to the quality of the product have been made following applications for variations. The statement should also include the currently authorised specifications for the active substance and the finished product, and the qualitative and quantitative composition in terms of the active substance(s) and the excipient(s). MA holders are asked to check that the composition, specifications and the references to test methods submitted with the application are those approved by the HPRA. Any revision of the specifications to bring them into line with current requirements, including pharmacopoeial standards, must be done by variation before submission of the renewal.

In addition the statement should confirm that the product conforms to current CHMP quality guidelines where relevant, e.g. Note for Guidance on Impurities: Residual Solvents (CPMP/ICH/283/95) and Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products (EMEA/410/01). Updated TSE certificates must be submitted by variation using the appropriate category in line with the Guideline on Dossier Requirements for Type IA and Type IB notifications.

If the MA holder is submitting updated stability data to fulfil commitments provided during previous regulatory activities, reference to the documentation should be made in the cover letter for the renewal application. When submitting updated stability studies, the MA holder should confirm that the formulation, packaging materials and analytical methods used are those previously approved, and include a conclusion based on the results of the stability studies.

3.6 Documentation validation checks

Applicants should ensure the accuracy of all documentation submitted, including the information provided in the application form.

Applications which do not include the required documents, including an addendum to the clinical overview in module 2 will not be validated.

Please see the HPRA Guide to Electronic Submissions – Human Medicines for details on sending the application to the HPRA.

Failure to respond or the submission of an incomplete response will result in the MA being considered withdrawn and the files closed. Any corrections to the product information required after it has been issued must be applied for using the variation procedure.