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Human Medicines Evaluation Division

Pre-submission checklist for annual renewal of conditional marketing authorisation applications

The purpose of this checklist is facilitating submission of complete and correct Annual Renewal Applications by marketing authorisation holders (MAHs).

Guidance for Marketing Authorisation Holders

The Agency strongly recommends that this checklist is used in advance of submission of Annual Renewal Applications. You should be able to answer "Yes" to every item listed below unless a specific point is not applicable ("n/a") to the application in question. Please note that this checklist should not be included in the submission.

Upon receipt of an Annual Renewal Application, the procedure manager proceeds to validate the documentation submitted in accordance with the checklist included below.

Issues identified during validation will be notified to the MAH via email. The MAH will be requested to provide responses to the issues raised within 5 working days. Delayed or insufficient responses may affect the timely start of the procedure.

Reference documents for further information:

- Regulation (EC) No 726/2004, Article 14(7)
- Regulation (EC) No 507/2006
- CHMP Guideline on Conditional Marketing authorisations
- Post-authorisation guidance on annual renewal of conditional marketing authorisations

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Annual Renewal of a conditional MA - validation checklist

The Annual Renewal application must be submitted at the latest 6 months before the MA expiry date[1]. Earlier submission could be envisaged, provided that it does not exceed 7 months in advance. Submission of Annual Renewal applications earlier than 7 month in advance of the MA expiry date will not be accepted by the Agency.

Module 1	Yes	N/A	Comments
1.0 Cover letter with the following documents attached (see boxes below):	☐		*[The cover letter is signed and dated by the person authorised to communicate on behalf of the MAH (as notified to the Agency), or a letter of authorisation for a new person is attached.]* *The Annual Renewal application is not an opportunity to notify the Agency of changes in contact persons, which should be notified separately as soon as they happen (see dedicated question under section 'Other post-authorisation activities: questions and answers' of the EMA published guidance: "How do I notify the EMA of changes to my Contact Persons specified in the application form")*
If not all presentations are to be renewed, it is clearly indicated in the cover letter and appended list of presentations is updated	☐	☐	*In cases where the MAH does not wish to renew certain product presentations, this should be clearly indicated in the cover letter and they should not be included in the appended list*.* **List of all authorised product presentations for which the renewal is sought in tabular format* *If applicable, list any presentation NOT to be renewed]*
A chronological summary table of **all** SOBs initially agreed, stating for each: • description • reference number (preferably SIAMED number) • due date • date of submission and procedure within which the SOB was submitted (if appropriate) • date when the obligation has been resolved (if applicable) • status	☐		

[1] In order to insert the correct date, go to the EC Pharmaceuticals - Community Register site, click on the product name and add 1 year to the date shown in column 'Close date procedure' allocated to *Centralised - Authorisation* under section 'European Commission procedures'.

A present/proposed table listing any changes introduced to the product information (incl. any minor linguistic amendment introduced for each language), if applicable	☐	☐	*[only if changes to the PI are proposed]*
1.3.1 Product Information	**Yes**	**N/A**	
<u>If changes proposed:</u> PDF version of EN annexes in the eCTD sequence Word version of EN annexes (Clean) Word version of EN annexes in tracking mode	☐ ☐ ☐	☐ ☐ ☐	*[If changes are proposed, updated PI should be provided:* *- WORD version (track-changes and 'clean')* *- pdf version]*
Affected Annexes: SmPC Annex II Labelling Package Leaflet	 ☐ ☐ ☐ ☐	 ☐ ☐ ☐ ☐	
<u>If no changes are proposed:</u> Word version of EN annexes (Clean)	☐	☐	*[Check that reference is made in the cover letter that no changes to the PI are proposed.]*
1.4 Information about the experts			
1.4.1 Information about the Expert – Quality (incl. signature + CV) – if applicable **1.4.2** Information about the Expert – Non-Clinical (incl. signature + CV) – if applicable **1.4.3** Information about the Expert – Clinical (incl. Signature + CV)	☐ ☐ ☐	☐ ☐	
1.8.2 EU-RMP (Risk Management Plan)			*[If SOB data submitted with the annual renewal warrant an RMP update, an updated RMP should be submitted.]* <<u>Updated RMP</u>: Version XX>
Updated EU-RMP provided as part of the submission <u>Changes proposed</u> EU-RMP provided as clean PDF version in the eCTD sequence EU-RMP provided in track-changes as Word document	☐	☐	*An RMP is not systematically required as part of the Annual renewal application. Two scenarios are possible:* *- Where there are no new data in the Renewal dossier justifying changes to the latest approved RMP and no recommended update to the RMP is to be implemented, an RMP update should not be included in the Renewal submission. In this case, the MAH should specify this in the cover letter and declare in the*

	☐ ☐	☐ ☐	*clinical overview that the current approved RMP does not require changes and remains applicable.* - *If an update of the RMP is proposed by the MAH as a consequence of data submitted with the Renewal application, section 1.8.2 should contain the updated RMP ('clean' version). In this case, a version of the RMP, highlighting the changes proposed by the MAH should be provided in Word format.*
Module 2	**Yes**	**N/A**	**Comments**
2.3 Addendum to Quality Overall Summary	☐	☐	*An Addendum to the Quality Overview is not systematically required as part of the annual renewal application. It should be provided only in case important new pharmaceutical data are available.*
2.4 Addendum to Non-Clinical Overview	☐	☐	*An Addendum to the Non-clinical Overview is not systematically required as part of the annual renewal application. It should be provided only in case important new non-clinical data are available.*
2.5 Addendum to Clinical Overview	☐		*A critical discussion should be provided within the Addendum to the Clinical Overview. It should address the current benefit/risk balance for the product on the basis of the data generated in SOBs and taking into account any other safety/efficacy data (including PSUR data) accumulated since the granting of the MA*
Expert report addressing the data submitted as well as the status of fulfilment of the SOBs and their impact on the overall benefit/risk balance of the medicinal product, in the form of a separate section in the clinical overview addendum, preferably containing the following information:	☐		*An **interim report** on the specific obligations should be included in a separate section in the clinical overview addendum. The interim report on the fulfilment of the specific obligations should include details for each specific obligation. The aim of this report is to inform about the status of fulfilment of specific obligations and the impact of data generated on the benefit risk-balance of the product. If data from a specific obligation is due at the time of annual renewal submission and have not been yet submitted, it can be included in the annual renewal submission dossier. Final reporting of clinical trials should follow the conventional format of study reports. Clinical Summaries and Clinical Study Reports should not be included in section 2.5, but in the respective dedicated eCTD Sections, see below. One single report should be submitted for the product including all remaining specific obligations. The structure and contents of the interim report will vary depending on the type of study and available data.*

Summary of information previously submitted to address ongoing SOBs	☐		*[This pertains to SOBs that are still in place. Information submitted previously that led to a complete fulfilment of a SOB should not be re-submitted.]*
Data submitted with the Annual Renewal to address outstanding SOBs	☐	☐	*[New summaries should be submitted in section 2.7 and clinical study reports in section 5.3.5 – see below]*
Critical evaluation of status of fulfilment of each pending SOB	☐		
2.7 Clinical Summary			
Updated clinical summaries provided with the application	☐	☐	*[Clinical summaries will generally need updating, as appropriate, when new clinical study reports are submitted.]*
Module 5	**Yes**	**N/A**	**Comments**
5.3.5 Clinical study reports (Reports of Efficacy and Safety Studies, as appropriate, submitted to fulfil SOs)			*[If data from a specific obligation is available in the form of a clinical study report for submission at the time of an annual renewal application, this should be submitted in Module 5 of such an application.]*
5.3.5.1 Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication	☐	☐	
5.3.5.2 Study Reports of Uncontrolled Clinical Studies	☐	☐	
5.3.5.3 Reports of Analyses of Data from More Than One Study	☐	☐	
5.3.5.4 Other Clinical Study Reports	☐	☐	

This checklist is published for transparency purposes and to facilitate submission of complete and correct annual renewal applications. This does not preclude that, during the actual validation of the submitted application, the Agency may identify other issues that could impact the validation outcome.