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Human Medicines Evaluation Division

Pre-submission checklist for annual re-assessment of a marketing authorisation under exceptional circumstances application

The purpose of this checklist is facilitating submission of complete and correct Annual Re-Assessment 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 Re-Assessment 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 Re-Assessment 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:

- Directive 2001/83/EC, Article 22 and its Annex I, Part II.6
- Regulation (EC) No 726/2004, Article 14(8)
- CHMP Guideline on procedures for the granting of a marketing authorisation under exceptional circumstances
- Post-authorisation guidance on annual re-assessment procedures

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Annual Re-Assessment of a MA under exceptional circumstances - validation checklist

The annual re-assessment application must be submitted on the anniversary date of the Commission Decision granting the Marketing Authorisation[1]. Flexibility in the submission date could however be envisaged (e.g. to synchronise the annual re-assessment submission with the submission of data from the SOBs). The annual re-assessment application submission could be adjusted within a maximum of +/- 2 months in such cases.

Module 1	Yes	N/A	Comments
1.0 Cover letter Signed by the contact person for the product or a letter of authorisation is attached **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 Re-assessment 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")*
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) • status	☐		
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] 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'.

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			
1.4.3 Information about the Expert – Clinical (incl. Signature + CV).	☐		
1.8.2 EU-RMP (Risk Management Plan)			*[If SOB data submitted with the annual re-assessment 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 Annual re-assessment applications. Two scenarios are possible:* *- Where there are no new data in the dossier justifying changes to the latest approved RMP, the RMP update should not be included in the submission. In such 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 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
2.5 Addendum to Clinical Overview			
The 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 Clinical Overview update or addendum, with the following structure (headings):			
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 Re-Assessment 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 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 re-assessment 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 re-assessment 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.