EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

3 April 2017
EMA/190616/2016 Rev. 1
Human Medicines Evaluation Division

Pre-submission checklist for 5-year renewal applications

The purpose of this checklist is facilitating submission of complete and correct 5-year 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 5-year 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 a 5-year 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.

MAHs are reminded of the requirement to submit specimens at the time of the 5-year Renewal Application. These are to be submitted **by post** to the Agency.

Reference documents for further information:

- Guideline on the processing of renewals in the centralised procedure (EC website – NTA - Volume 2C)
- Application form for renewal of a marketing authorisation (EC website – NTA - Volume 2C)
- Renewal Post-Authorisation Guideline (EMEA website)
- Checking process of mock-ups and specimens of outer/immediate labelling and package leaflets of human medicinal products in the centralised procedure (EMA/305821/2006/Rev.2) http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004891.pdf

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

Renewal validation checklist

The Renewal application must be submitted at the latest 9 months in advance of the MA expiry date[1]. Earlier submission could be envisaged, provided that it does not exceed 11 months in advance. Submission of Renewal applications earlier than 11 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	☐		
1.2 Renewal application form and annexes			
Application Form (AF) - Contact person for the product	☐		*[The AF (and cover letter) is signed 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 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]*
Details of contact persons: – QP in the EEA for pharmacovigilance – contact person in the EEA for product defects and recalls – contact person for scientific service in the EEA	☐ ☐ ☐		*[The Renewal application is not an opportunity to notify the Agency of changes in contact persons.* *The official form (Q.4. 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") should be provided by the MAH when a change takes place]*
Chronological list of conditions and specific obligations submitted since granting of the MA or last renewal indicating scope, status, date of submission and date when resolved	☐	☐	
Revised list of remaining conditions and specific obligations (where appropriate)	☐	☐	

[1] In order to insert the correct date, go to the EC Pharmaceuticals - Community Register site, click on the product name and add 5 years to the date shown in column 'Close date procedure' allocated to *Centralised - Authorisation* under section 'European Commission procedures'.

Chronological list of all post-authorisation submission since granting the MA or since the last renewal: a list of all approved or pending Type IA/IB and Type II variations, Extensions, Art 61(3) Notifications, USR, and PSURs/PBRER, giving the procedure number (where applicable), date of submission, date of approval (if approved) and brief description of the change.	☐		
List of EU Member states/Norway/Iceland where the product is on the market with indication for each country which presentations are marketed and the launch date.	☐		
A statement, or when available, a certificate of GMP compliance, not more than three years old, for the manufacturer(s) of the medicinal product listed in the application issued by an EEA competent authority or MRA partner authority. A reference to the Community EudraGMP database, if available will suffice.	☐		
For manufacturing sites of the medicinal product not located in the EEA or in the territory of an MRA partner, a list of the most recent GMP inspections carried out indicating the date, inspection team and outcome	☐	☐	
Declaration by the Qualified Person (QP) of each of the manufacturing authorisation holders (i.e. located in the EEA) listed in the application form where the active substance is used as a starting material Declaration by the Qualified Person (QP) of the manufacturing authorisation holder(s) listed in the application as responsible for batch release.	☐		*[In accordance with Article 46(f) of Directive 2001/83/EC, manufacturing authorisation holders are required to use as starting materials only active substances which have been manufactured in accordance with the detailed guidelines on good manufacturing practice for starting materials as adopted by the Community.* *Declarations should state that all the active substance manufacturer(s) referred to in the application form operate in compliance with the detailed guidelines on good manufacturing practice for starting materials.]*
1.3.1 Product Information	**Yes**	**N/A**	
Word version of EN annexes clean	☐		
Word version of EN annexes in tracking mode if changes to the PI are proposed as part of the Renewal	☐	☐	*[If changes are proposed, updated PI in track-changes (WORD) and 'clean' (WORD and pdf) should be provided].*
1.4 Information about the experts + signature + CV	**Yes**	**N/A**	
1.4.1 Quality expert	☐	☐	*[CV and expert's signature need to be provided]*
1.4.2 Pre-Clinical expert	☐	☐	*[CV and expert's signature need to be provided]*
1.4.3 Clinical expert	☐		*[CV and expert's signature need to be provided]*
1.8			
1.8.2 Risk Management Plan	**Yes**	**N/A**	
The module has been provided	☐	☐	*[Submission of an RMP is not mandatory, therefore the option 'not applicable' can be ticked, given that when there are no new data justifying changes to the latest approved RMP, a declaration is included in the clinical overview and a*

			confirmation that the current approved RMP remain unchanged and applicable. Where there is no RMP for the medicinal product, this should be clearly stated in the cover letter.]* *[If an updated RMP is submitted, it should also be provided in track changes as a working (WORD.doc) version.]*
2.3 Addendum to Quality Overall Summary	☐		
The following required declarations and statements should be included: – Declaration of compliance with Art. 16(1) of Reg. (EC) No 726/2004, which obliges the MAH to "... take account of technical and scientific progress and introduce any changes that may be required to enable the medicinal products to be manufactured and checked by means of generally accepted scientific methods".	☐		*(No updating of Module 3 quality data is expected with the Renewal. It is a legal obligation of the MAH to keep Module 3 updated on an on-going basis throughout the life of the product using variation procedures*
The following 3 should also be included: – Confirmation that all changes relating to the quality of the product have been made following applications for variations and that the product conforms to current CHMP Quality guidelines. – currently authorised specifications for the active substance and the finished product (with date of latest approval and procedure number) – qualitative and quantitative composition in terms of the active substance(s) and the excipient(s) (with date of latest approval and procedure number)	☐ ☐ ☐		*[These three indents should be provided as part of Module 2.3*
2.4 Addendum to Non-clinical Overview	**Yes** ☐	**N/A** ☐	*An Addendum to the non-clinical Overview is not systematically required as part of the renewal application.* *When new data are submitted in the non-clinical Addendum, a critical discussion must be submitted as part of the renewal application supporting the benefit/risk balance re-evaluation for the product taking into account any new non-clinical data accumulated since the initial MA or the last renewal, or any relevant new information in the public domain.* *In case no new non-clinical data have been gathered since the initial MAA or since the last renewal, this should be clearly stated in the Addendum to the Clinical Overview*.
2.5 Addendum to Clinical Overview	☐	☐	
Check of Overview being satisfactory: – worldwide marketing status – actions taken for safety reasons – significant changes made to the reference information,	☐ ☐ ☐		*A critical discussion should be provided within the Addendum to the Clinical Overview. It should address the benefit/risk balance for the product at the time of the application for the*

– differences between the reference information and the SmPC proposal – estimated exposure – significant safety and efficacy findings – literature review – risk-, benefit- and B/R evaluation – late-breaking information – data in summary tabulations of Serious adverse events – overview of signals – signal and risk evaluation – information on patterns of medication errors – statement regarding no non-clinical issues (if no Addendum to Non-clinical Overview is submitted) – * statement regarding the fact that the current approved RMP remains unchanged and applicable (if RMP is in place, but no update is submitted)	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	☐	*Renewal, on the basis of the Periodic Safety Update Reports (PSUR)/ Periodic Benefit Risk Evaluation Report (PBRER) data and safety/efficacy data accumulated since the granting of the MA or since the last renewal, making reference to relevant new information in the public domain.* *The discussion should clearly reflect the data previously included in the previous PSURs/PBRER and the 'delta' constituted by new data that have emerged since the DLP of the last PSUR/PBRER up to the DLP of the renewal.*
Clinical Expert Statement (confirmatory statements – as reflected in Annex II of the Guideline on the processing of renewals in the centralised procedure)	☐		*The Clinical Expert Statement should:* *-Confirm that no new clinical data are available which change or result in a new risk/benefit balance evaluation.* *- Confirm that the product can be safely renewed at the end of a 5-year period for an unlimited period, or any action recommended or initiated should be specified and justified.* *- Confirm that the authorities have been kept informed of any additional data significant for the assessment of the benefit/risk balance of the product concerned.* *- Confirm that the product information is up to date with the current scientific knowledge including the conclusions of the assessments and recommendations made publicly available on the European medicines web-portal.*
2.5 Addendum to Clinical Overview – history of PhV system inspections	☐	☐	*History of pharmacovigilance system inspections should include the following elements: date, inspecting authority, site inspected, type of inspection and if the inspection was product specific, the list of products concerned.* *In addition an analysis of the impact of the findings overall on the benefit/risk balance of the medicinal product should be provided.*

This checklist is published for transparency purposes and does not preclude that, during the actual validation of the submitted application, the Agency may identify other issues to be addressed by the MAH.