EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Standard operating procedure

Title: Preparation of an initial European Public Assessment Report (EPAR) for a human medicinal product following positive or negative opinion		
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1. Purpose

The purpose of this SOP is to provide Product Team Leaders (PTLs) and PTL secretaries in the Human Medicines Development and Evaluation (H) unit with guidance on the procedure for the preparation of the initial European Public Assessment Report (EPAR) from the adopted CHMP Assessment Report (AR) following initial marketing authorisation applications with a positive or a negative opinion (refusal of marketing authorisation).

It does not cover the preparation of an EPAR following the adoption of an opinion for a procedure under article 58 of Regulation (EC) 726/2004, or for the preparation of an EPAR following the withdrawal of an application.

2. Scope

This SOP applies to the Safety and Efficacy of Medicines (H-SE) and Quality of Medicines (H-QM) sectors in the H Unit.

3. Responsibilities

It is the responsibility of each Section Head, Head of Sector and Head of Unit to ensure that this procedure is adhered to within their own Section/Sector/Unit. The responsibility for the execution of a particular part of this procedure is identified in the right-hand column of 9. Procedure.

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4. Changes since last revision

Revision to implement changes following the reorganisation of the Agency. Clarification that scope of the SOP is limited to the initial EPAR only. Furthermore, guidance added for divergent position and Annex IV of the CHMP opinion. Finally, use of MMD and SIAMED in the process has been included.

5. Documents needed for this SOP

Template 1: Communication to the applicant asking for comments/proposals on confidentiality issues

Template 2: Reminder e-mail to company

Template 3: Cover page for EPAR DRAFT I in 1st CHMP post-mail

Template 4: EMA Sign off of the English EPAR

Template 5: Letter to the applicant with final EPAR

Templates 1 - 5 are on the X: drive under Templates/Other/H – EPAR.

Template 6: TS - NEW EPAR Human

Template 7: TS - Refusal EPAR

Templates 6 - 7are available under Word, File, New, Transmission Slips

6. Related documents

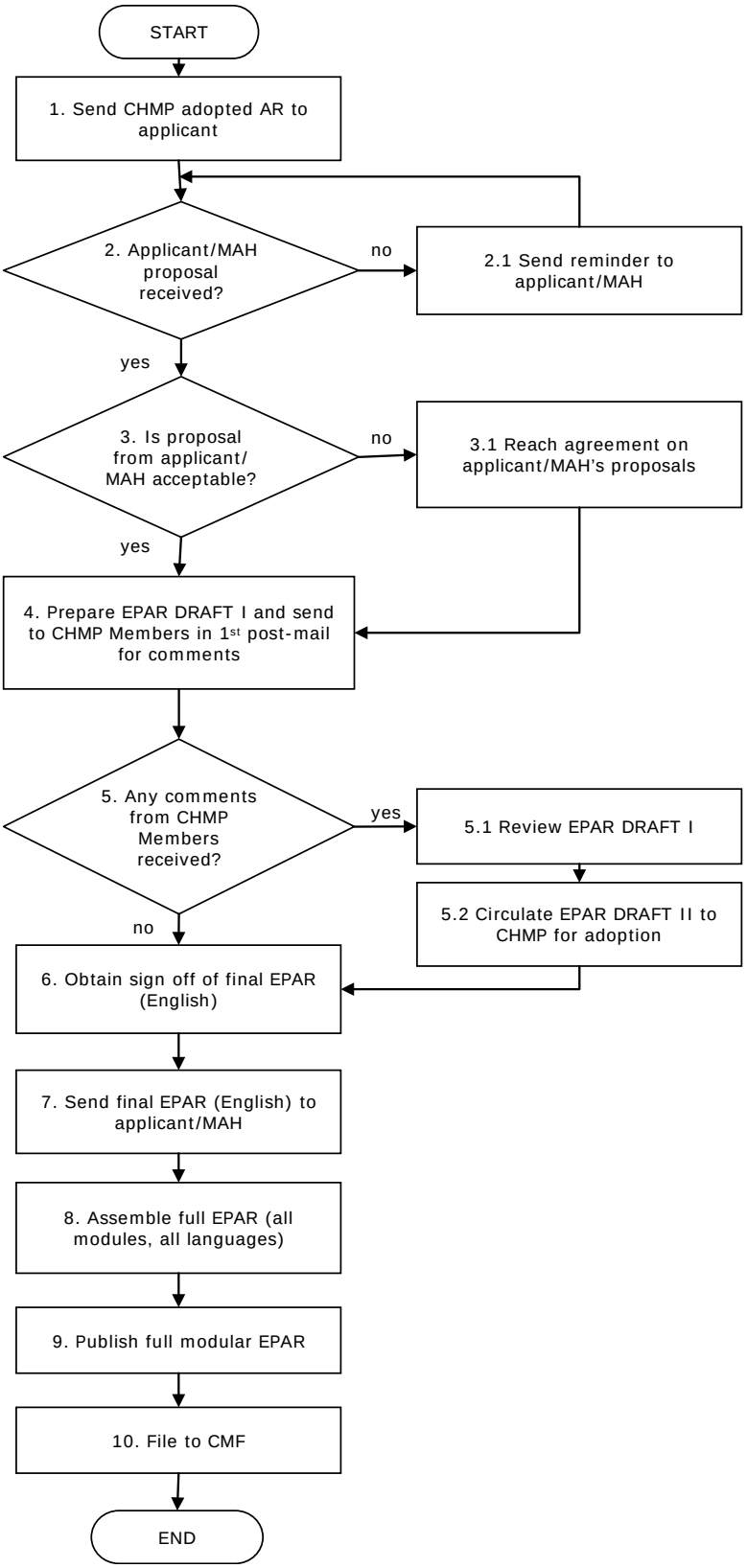
1. Reflection paper on the publication of CHMP negative opinion and refusal of marketing authorisation applications for human medicinal products (EMA/311355/2005) http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004188.pdf
2. SOP/H/3131 - Preparation and updates of EPAR summaries by the Medical Information Sector
3. SOP/H/3012 - Updating of the European Public Assessment Report for a human medicinal product
4. Principles to be applied for the deletion of commercially confidential information for the disclosure of EMEA documents (EMA/45422/2006) http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004043.pdf

7. Definitions

AR	Assessment Report (the CHMP Assessment Report with the confidential information deleted)
CD	Commission Decision
CdT	Centre de Traduction (Luxembourg translation centre)
CHMP	Committee for Medicinal Products for Human Use
CHMP AR	CHMP Assessment Report (the Assessment Report adopted by the CHMP at the time of the Opinion)
CMF	Core Master File

DREAM	Document Records Electronic Archive Management
EMA	European Medicines Agency
EPAR	European Public Assessment Report
H-QM	Quality Sector in the Human Medicines Development and Evaluation Unit
H-SE	Safety and Efficacy Sector in the Human Medicines Development and Evaluation Unit
HoS	Head of Sector
MMD	Managing Meetings Documents
P-MI	Medical Information Sector in the Patient Health Protection Unit
PTL	Product Team Leader
PTM	Product Team Member
SIAMED	Procedure tracking database
ToD	Table of decisions
Q&A	Question-and-answer document
V-PD-DIS	Document and Information Services Section in the Product Data Management Sector in the Veterinary Medicines and Product Data Management Unit

8. Process map / flow chart



9. Procedure

Step	Action	Responsibility
	Day 1 after adoption of the opinion by CHMP	
1.	**Send out CHMP AR to the applicant / MAH** Send the adopted CHMP AR (which should include the divergent position(s) if any copied and pasted without signatures from the opinion as an appendix) by Eudralink, requesting the applicant/MAH to identify those issues that are considered to be commercially confidential and to make a proposal including justifications for deletions/alternative wording, within 15 calendar days. (*Template 1*) In case of a negative opinion, when to send this depends on whether the applicant ask for a re-examination: • if the applicant/MAH decides not to ask for a re-examination: send the document as soon as the applicant has notified the Agency that they will not appeal; • if a re-examination takes place: send the document on the day after adoption of the CHMP opinion on the re-examination procedure. **Note:** In the case of a positive CHMP Opinion[1] for an initial authorisation, a medical writer in P-MI will use the adopted CHMP AR and Product information to prepare a draft EPAR Summary by Day 35 after adoption, in time for the post-mail of the 1st CHMP after Opinion. (see SOP/H/3131)	PTL/PTL secretary
2.	**Day 15 - Applicant's proposal received?** If the applicant's proposal has been received go to Step 3. If the applicant's proposal has not been received go to Step 2.1.	PTL secretary
2.1	Send e-mail reminder(s) until proposal is received (Template 2). Go back to Step 2.	PTL secretary
3.	**Day 15-22 – Is applicant's proposal acceptable?** Check the acceptability of this proposal and justifications with the: • PTM (H-SE or H-QM), • Section Head. Only confidential information, factual errors and grammar mistakes should be amended. Consult the Rapporteur only if the proposals for deletion impact on the scientific integrity of the report (e.g.	PTL

[1] For negative opinions a q-and-a document will already have been prepared by P-MI and tabled at the time of the CHMP Opinion and CHMP AR.

Step	Action	Responsibility
	change to data tables). If the proposal is acceptable go to Step 4. If the PTL is unsure that the proposal is acceptable go to Step 3.1.	
3.1	**Day 22-25 – Reach agreement on applicants proposals** Questions regarding proposals from the applicant need to be discussed with Section Head or responsible PTM (H-SE or H-QM) and P-MI. Involvement of the Legal sector may be sought at this stage. Organise internal review, record outcome and inform applicant of outcome. Continue with Step 4.	PTL
4.	**Day 35 - Prepare EPAR DRAFT I and send to CHMP members in CHMP post-mail for adoption**[2]	
	a. Receive EPAR Summary from P-MI (this is received only in case of a positive opinion for an initial authorisation –see SOP/H/3131).	PTL/PTL Secretary
	b. Prepare the AR Check the version of the AR to ensure that all confidentiality issues have been resolved. If the PTL is in the H-SE sector, he/she should seek confirmation from the PTM in the H-QM sector and vice versa (if PTL is in the H-QM sector, he/she should seek confirmation from the PTM in the H-SE sector). The document should show clearly what amendments/deletions are being carried out and the reasons for them.	PTL
	c. Assemble the EPAR DRAFT I for the post-mail of the 1st CHMP after Opinion: • EPAR Summary (positive opinion) or Q&A on refusal (negative opinion) – this should be the latest Q&A (i.e. reflecting the re-examination if appropriate) • AR And add the **cover page** (*Template 3*).	PTL secretary
	d. Table EPAR DRAFT I in MMD for post-mail and inform the CHMP secretariat for inclusion in the **CHMP ToD** requesting **CHMP comments** on draft EPAR to be sent to the PTL within 10 calendar days (indicate deadline on cover sheet and in CHMP Agenda).	PTL secretary

[2] Detailed information for these steps can be found in the 'Guidance on the handling of files for new EPARs – Human products' (front pages, file naming) *(related document 3)*.

Step	Action	Responsibility
5.	**Day 45 – Any CHMP comments received on EPAR DRAFT I?**	
	Check if comments received from CHMP members.	PTL/PTL secretary
	If no comments have been received, go to Step 6.	
	If comments have been received go to Step 5.1.	
5.1	**Day 48 - Review EPAR DRAFT I**	
	Liaise with the CHMP members who have commented and with the Rapporteur to discuss the issue(s) raised (e-mail/phone) involving PTM as appropriate. Prepare the EPAR DRAFT II showing the comments raised.	PTL
5.2	**Day 49 - Circulate EPAR DRAFT II**	
	Inform CHMP Secretariat that an EPAR DRAFT II will be tabled for adoption in MMD for the 2nd CHMP after Opinion.	PTL secretary
	Table EPAR DRAFT II in MMD.	PTL secretary
	Continue with Step 6.	
6.	**Day 45 or Day 60 - EMA sign-off of final EPAR (English)**	
	Once the EPAR DRAFT I has been adopted by written procedure (at day 45) or EPAR DRAFT II has been adopted by CHMP (at day 60), the final EPAR - public assessment report is finalised for publication by:	PTL
	1. accepting all changes and deleting all comments to prepare a clean version of the text,	PTL/PTL secretary
	2. deleting names and details of peer reviewer, assessors and PTL and all Annexes and Appendices (except for the divergent positions annex if any), Other parts should also be deleted as appropriate. For an opinion for initial authorisation, always delete from the CHMP AR the Product Information summary table.	PTL Secretary
	3. editing the front page to indicate that this is a public document with all commercially confidential information removed,	PTL Secretary
	4. re-running the Table of Contents.	PTL Secretary
	Send final EPAR - public assessment report and summary together to HoS for sign-off. (*Template 4*). This is an internal scientific sign off to confirm and record that the public assessment report is suitable for publication (all commercially confidential information has been deleted) and that the summary is fully aligned with the public assessment report.	

Step	Action	Responsibility
7.	**Day 46 or Day 61 - Send final EPAR (English) to applicant / MAH** Send the final EPAR – public assessment report and the corresponding EPAR – Summary for the public to applicant (*Template 5*).	PTL secretary
8.	**Between Day 1 and CD date - Assemble the other components of the full EPAR for publication**[3] The text below outlines the steps for the components for full EPAR. **EPAR** a. Create Product Overview from SIAMED. b. Request from translationsrequests@ema.europa.eu (V-PD-DIS) the translations in all EU languages by the CdT of EPAR - Summary for the public and Annex IV - the scientific conclusions and grounds if outcome of assessment of the claim is negative. This can only take place once step 5. (or 6.) has been completed. c. Obtain (from applicant) translations in all EU languages of: • Annex A (EPAR – All authorised presentations). • adopted PI (EPAR – Product Information). • Annex 127a (EPAR - Conditions imposed on member states for safe and effective use), if applicable. • Annex IV (EPAR – conclusions on MA under exceptional circumstances or conditional approval, accepted derogation on similarities, request for 1-year marketing protection), if applicable and if the assessment of the claim is positive. **Orphan product**: if the product has an orphan designation, the COMP document summarising the review of the designation must be linked to and from the EPAR – public assessment report at the time of publication of the full EPAR. This document will have been been prepared and published by the Orphan Drugs Section. **Refusal EPAR** a. Request from translationsrequests@ema.europa.eu (V-PD-DIS) the translations of Q&A on Refusal in all EU languages by the CdT.	PTL secretary PTL secretary PTL secretary PTL secretary PTL secretary
9.	**CD date + 15 days – Publish full EPAR** The documents signed off at step 6, as well as all the documents and translations processed at Step 8 are sent off for web	PTL Secretary

[3] Detailed information for these steps can be found in the 'Action list for product secretaries' under Word, File, New (timings, liaison with Applicants) and the 'Guidance on the handling of EPAR files – Human products' (related document 5).

Step	Action	Responsibility
	publication using suitable transmission slip (*template 6*/*template 7*). All paper documents relating to the corresponding electronic files submitted for publication must be checked before the sign off starts. **Note**: Publication can only take place once the Commission Decision has been issued, and should be within 15 days of the issue of the CD.	PTL secretary
10.	**On publication of EPAR** Commit to Core Master File all final published files in DREAM. Close the application in SIAMED II: see guidance below Closing an Application EMA/459672/2011 https://docs.eudra.org/webtop/drl/objectId/090142b2819623f7	PTL secretary

10. Records

EPARs and correspondence relating to them are part of the Core Master File and should be kept according to SOP/PDM/1004.

EPAR publication is tracked by P-MI in the EPAR tracker database.