EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Standard operating procedure

Title: Review of the period of market exclusivity of orphan medicinal products in accordance with Art. 8(2) of Regulation (EC) 141/2000		
Status: **PUBLIC**		Document no.: SOP/H/3526
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Signature: [On file]	Signature: [On file]	Supersedes: N/A
Date: 12.06.2017	Date: 12.06.2017	TrackWise record no.: 5179

1. Purpose

To describe the procedure for review of the period of market exclusivity (ME) of orphan medicinal products.

2. Scope

This SOP applies to:

- Committees Secretariat Service in Committees and Inspections Department in Inspections, Human Medicines Pharmacovigilance and Committees Division
- Legal Department
- Medical and Health Information Service in Communication Department in Stakeholders and Communication Division
- Orphan Medicines Office in Product Development Scientific Support Department in Human Medicines Research and Development Support Division
- Regulatory Affairs Office in Regulatory, Scientific and Regulatory Management Department in Human Medicines Evaluation Division

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3. Responsibilities

It is the responsibility of each Service/Office Head to ensure that this procedure is adhered to within their Service/Office. The responsibility for the execution of a particular part of this procedure is identified in the right-hand column of section 9.

4. Changes since last revision

New SOP.

5. Documents needed for this SOP

All templates are available on X:\Templates\Others\H-Orphan Medicines

Template 1 - Review of ME receipt of MS notification

Template 2a - Review of ME - letter to EC on MS notification

Template 2b - Review of ME- letter to MAH on MS notification

Template 3a - Review of ME - assessment report

Template 3b - Review of ME - presentation

Template 3c - Review of ME - messages for sending LOQ to MAH

Template 4 - Review of ME - COMP Co-expert comments

Template 5 - Review of ME - positive opinion

Template 6a - Review of ME - negative opinion

Template 6b - Review of ME - negative opinion to MAH

Template 6c - Review of ME - notification to MAH of negative opinion to EC

Template 7 - Review of ME - positive opinion after appeal

Template 8 - Review of ME - negative opinion after appeal

Template 9a - Review of ME - opinion to EC

Template 9b - Review of ME - opinion to MAH

6. Related documents

- Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products

  http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2000:018:0001:0005:en:PDF

- Guideline on aspects of the application of Article 8(2) of Regulation (EC) No 141/2000 of the European Parliament and of the Council: Review of the period of market exclusivity of orphan medicinal products (2008/C 242/07)

  http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2008:242:0008:0011:EN:PDF

- SOP/H/3049 on orphan medicinal product designation

- SOP/H/3371 on preparation and publication of the public assessment of opinion on the review of orphan designation at the time of marketing authorisation
- WIN/H/3047 on orphan electronic product folders
- Listing for tracking procedures for review of period of market exclusivity of orphan medicinal products is available in DREAM:

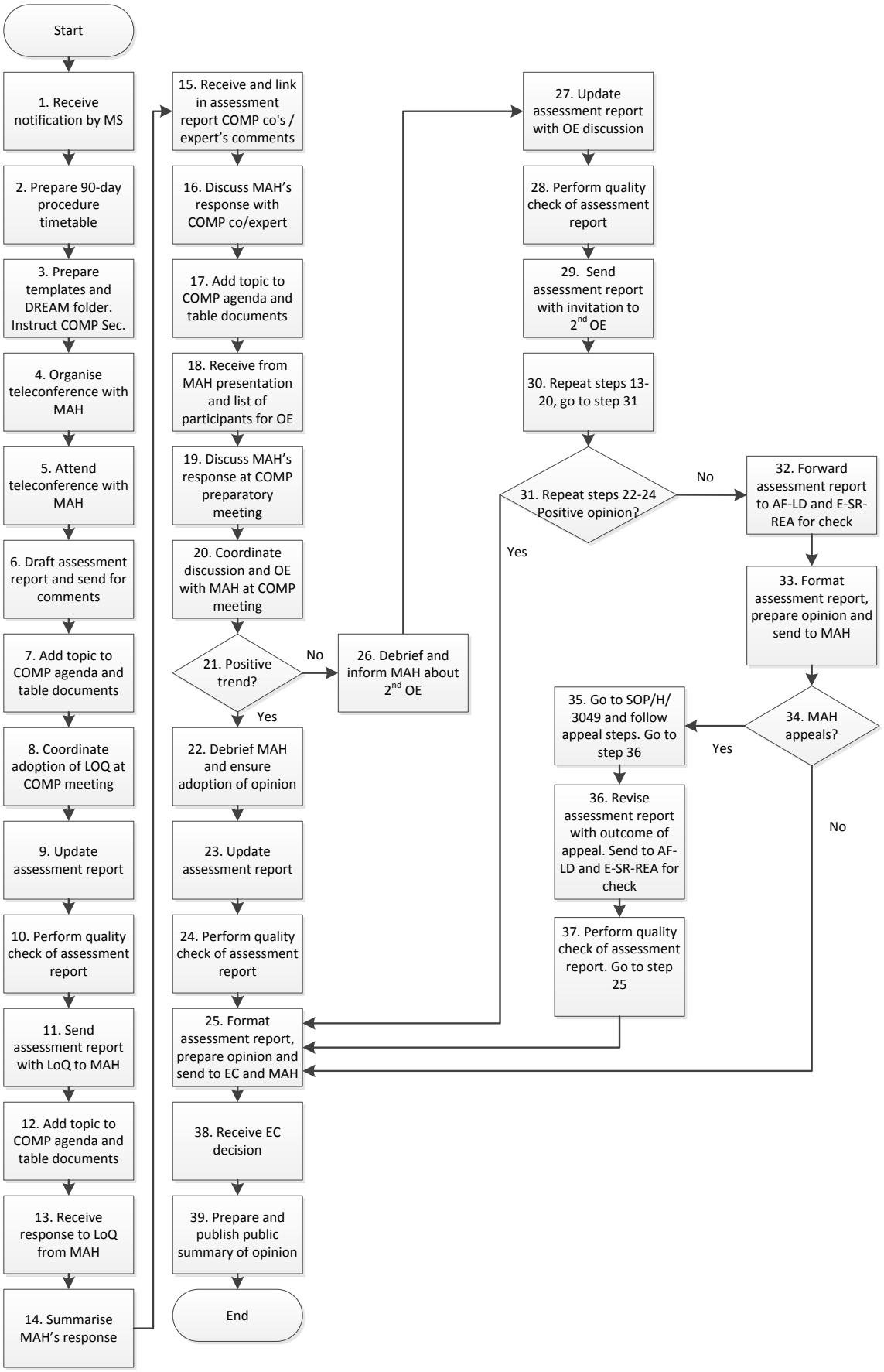
  05. External Guidelines and Procedural Advice/05.2 Regulatory and Procedural Advice/1. Human/1.08 Orphans/Article 8(2)

7. Definitions

AF-LD	Legal Department
COMP	Committee for Orphan Medicinal Products
COMP Co	COMP Co-ordinator
COMP Sec	COMP Secretariat (in P-CI-SCS)
D-DS-OME	Orphan Medicines Office in Product Development Scientific Support Department in Human Medicines Research and Development Support Division
DREAM	Document records electronic archive management
E-SR-REA	Regulatory Affairs Office, Regulatory, Scientific and Regulatory Management Department in Human Medicines Evaluation Division
EC	European Commission
Eudralink	European medicines regulatory network's secure file-transfer system used for exchanging information for regulatory purposes
LoQ	List of questions
Line listing	OME office listing for tracking procedures for reviews of period of market exclusivity of orphan medicinal products
MA	Marketing authorisation
MAH	Marketing authorisation holder
ME	Market exclusivity
MHI writer	Medical writer (in S-CO-MHI)
MMD	Managing meeting documents system
MS	Member State
OD database	Orphan drugs database (in D-DS-OME)
OE	Oral explanation
OME Asst	Assistant (in D-DS-OME)
OME Co	Co-ordinator (in D-DS-OME)
OME HoO	Head of Orphan Medicines Office (in D-DS-OME)

P-CI-SCS	Scientific Committees Secretariat Service, Committees and Inspections Department in Inspections Human Medicines Pharmacovigilance and Committees Division
PSO	Public assessment of opinion
S-CO-MHI	Medical and Health Information Service, Communication Department in Stakeholders and Communication Division

8. Process map(s)/ flow chart(s)



9. Procedure

- *All messages containing confidential information must be sent via Eudralink.*
- *Product related correspondence must be saved in relevant product folder in DREAM.*
- *Unless no longer available, COMP Co and OME Co remain the same as per review of orphan designation procedure.*

Step	Action	Responsibility
	Pre-assessment	
1	• Receive notification by MS that at least one of designation criteria of the orphan medicinal product may no longer be met. • Confirm receipt (template 1). If not provided, request written justification from MS. • Check pre-requisites of the request are met in line with legislation e.g. time of request. • Where OME Co at time of initial designation/maintenance is no longer available, coordinate appointment of new OME Co.	OME HoO
2	• Prepare 90-day procedure timetable for start at forthcoming COMP meeting according to following guide: Day 1 – start of procedure and adoption of LoQ for Step 1 (review of initial designation criteria) and Step 2 (return on investment assessment) Day 30 - preliminary COMP discussion as required Day 60 - OE by MAH for Step 1 LoQ and adoption of positive opinion on the maintenance of orphan criteria, if the case or, if applicable, discussion with MAH on Step 2. Day 90 - Step 2: 2nd OE by MAH, adoption of COMP opinion. • Inform in writing EC (template 2a) and MAH (template 2b) about procedure providing MS' reasons for triggering Art. 8(2) and procedure timetable.	OME-co
3	• Prepare templates of assessment report (template 3a) and presentation (template 3b). • Create Art. 8(2) subfolder in DREAM product folder and save relevant correspondence and templates. • Forward link to OME Co. • Update OD database and review of ME listing. • Link relevant documents to forthcoming COMP meeting folder. • Instruct COMP Sec to add topic in COMP meeting agenda.	OME Asst
4	Upon request, organise teleconference with MAH to discuss	OME Asst

Step	Action	Responsibility
	procedural steps.	
5	Attend teleconference with MAH.	OME Co
6	• Draft assessment report implementing MAH justification. • Prepare slides for COMP plenary.	OME Co
7	• Add topic to forthcoming COMP meeting agenda for discussion and appointment of COMP Co(s) and expert(s). • Table in MMD relevant documents linked in COMP meeting folder for mailings.	COMP Sec
	Assessment	
8	At day 1 COMP meeting present procedure timetable to the COMP and coordinate discussion and adoption of LoQ to cover both Step 1 and Step 2.	OME Co
9	Update assessment report following COMP discussion.	OME Co
10	Perform quality check of assessment report with LoQ.	OME HoO
11	• Send assessment report with LoQ to MAH informing about deadline for response (3 weeks prior to day 60 COMP meeting) and including invitation to OE (template 3c). • Update OMP database and review of ME listing.	OME Asst
12	• Add topic to forthcoming day 30 COMP meeting agenda for potential discussion at day 30 and to day 60 COMP agenda for OE. • Table in MMD relevant documents linked in COMP meeting folder for mailings.	COMP Sec
13	• Receive response to LoQ from MAH, link in assessment report and save with version label. • Send to COMP Co for comments attaching template 4 (in case MAH didn't send response directly to COMP Co).	OME Asst
14	• Summarise MAH's response to LOQ and comment on maintenance of designation criteria in assessment report. • If needed also send assessment report to expert(s) attaching template 4.	OME Co
15	Receive comments from COMP Co and expert(s) and link in assessment report.	OME Asst
16	• Discuss MAH's response with COMP Co and expert(s) (if applicable) via telephone or email. • Update assessment report if necessary.	OME Co

Step	Action	Responsibility
17	• Add topic to next COMP meeting Agenda for OE by MAH. • Table in MMD relevant documents linked in COMP meeting folder for COMP mailings.	COMP Sec
18	• Receive from MAH presentation and list of participants for OE. • Link presentation to COMP meeting folder. • Forward OE information to COMP Sec.	OME Asst
19	Present and discuss MAH's response at COMP preparatory meeting	OME Co
20	Coordinate COMP discussion and OE with MAH at COMP meeting (firstly for Step 1 and on Step 2 only when applicable). MAH is not required to address Step 2 before Step 1 is concluded, however MAH can discuss response to Step 2 LoQ during the same plenary.	OME Co
21	• If COMP trend is positive, go to step 22. • If COMP trend is negative, go to step 26.	OME Co
22	• Debrief MAH on outcome of COMP discussion. • Ensure adoption of grounds for opinion.	OME Co
23	Update assessment report following OE and COMP discussion.	OME Co
24	Perform quality check of assessment report.	OME HoO
25	• Format assessment report and save with label as major version. • Prepare COMP opinion according to assessment report (template 5 or template 6a, for post-appeal template 7 or template 8). • Send COMP opinion and assessment report to EC (template 9a) and to MAH (template 9b, use template 6c if MAH failed to appeal). • Update OD database and review of ME listing, go to step 38.	OME Asst
26	Debrief and inform MAH about 2nd discussion at the next COMP meeting to conclude on Step 2.	OME Co
27	After COMP meeting update assessment report with OE discussion for sending to MAH with invitation to 2nd oral hearing.	OME Co
28	Perform quality check of assessment report.	OME HoO
29	Format and send assessment report with invitation to 2nd OE. (major version with label "for 2nd OE discussion") to MAH informing about deadline for sending additional data in support to Step 2 discussion (2 weeks before next - day 90 COMP meeting) (template 4a).	OME Asst

30	Repeat steps 13-20, go to step 31.	OME Co / OME Asst
31	• Repeat steps 22-24. • If COMP opinion is positive, go to step 25. • If COMP opinion is negative, go to step 32.	OME Co
32	• Forward assessment report with grounds for negative opinion to AF-LD and E-SR-REA for check. • Inform EC about COMP negative opinion.	OME Co
33	• Format assessment report and save with label and as major version. • Prepare COMP negative opinion (template 6a) according to assessment report. • Send COMP negative opinion and assessment report to MAH informing on possibility to appeal within 90 days of receipt of opinion (template 6b).	OME Asst
34	• Receive response from MAH. • If MAH appeals, go to step 35. • If MAH does not appeal, go to step 25.	OME Co/OME Asst
	Appeal	
35	• Go to SOP/H/3049 and follow steps in appeal phase. • Return to this SOP and go to step 36.	OME Co/OME Asst
36	• Revise assessment report with outcome of appeal. • Forward assessment report with grounds for appeal opinion to AF-LD and E-SR-REA for check.	OME Co
37	Perform final quality check of assessment report, go to step 25.	OME HoO
	Post EC decision	
38	• Receive from EC decision adoption message. • Save correspondence in DREAM. • Update OD database and reivew of ME listing.	OME Asst
	Public summary of opinion	
39	Prepare and publish public summary of opinion following steps in SOP/H/3371	MHI writer/ OME Co/ OME HoO/ OME Asst

10. Records

Records produced from this procedure are stored in accordance with WIN/H/3047.

Review reports are versioned and labelled for tracking procedural steps and electronic verification process. Opinions are labelled for recording final version and possible correction, revisions and corrigenda as applicable. Detailed labelling and versioning instructions are available in Cabinets/14. Working areas/14.01 D-Division/02. D-DS Activities/D-DS-OME Activities/Section activities/Templates and DREAM labels.