EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Standard Operating Procedure

Title: Orphan Medicinal Product Designation and Maintenance		
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1. Purpose

To describe the procedure for:

- The validation and evaluation of applications for orphan medicinal product designation and amendment of an existing orphan medicinal product designation;
- The review of the orphan designation at the time of an initial application for marketing authorisation of an orphan medicinal product, or an extension of indication;
- The review of the market exclusivity period of orphan medicinal products in accordance with Art. 8 (2) of Regulation (EC) 141/2000.

2. Scope

This SOP applies to the European Medicines Agency relevant scientific areas for human medicinal products, management of scientific committees' service and legal/regulatory advice service.

3. Responsibilities

It is the responsibility of the European Medicines Agency to adhere to the processes described in this document

4. Changes since last revision

New standard operating procedure.

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5. Documents needed for this SOP

Procedural advice for submitting an application for orphan medicinal product designation - Guidance for sponsors

Procedural advice for post-orphan medicinal product designation activities - Guidance for sponsors

6. Related information

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

Guideline on the format and content of applications for orphan medicinal product designation.

Orphan designation: research and development.

Applying for marketing authorisation: orphan medicines.

Market exclusivity: orphan medicines.

Regulatory and procedural guidance available.

7. Definitions

COMP	Committee for Orphan Medicinal Products
EC	European Commission
MAH	Marketing Authorisation Holder
OMAR	Orphan Maintenance assessement report
WOMAR	Withdrawal orphan maintenance assessmenrt report

8. Records

Records produced from the procedures described in this document are stored in the European Medicines Agency customer relationship management and document repository systems.

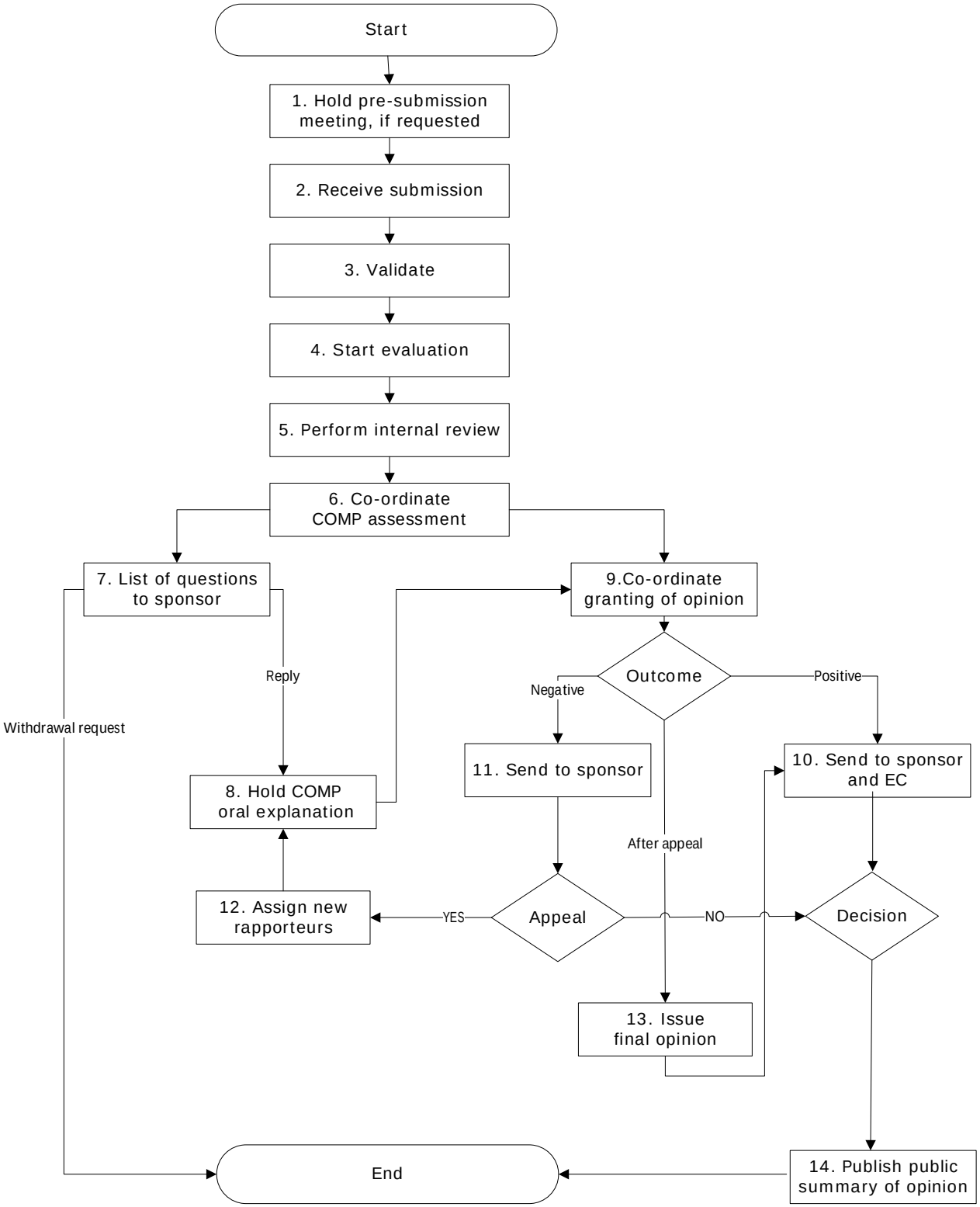
9. Procedures

9.1 Procedure for orphan medicinal product designation and amendment of an existing orphan medicinal product designation

Step	Action
1	Hold pre-submission meeting, if requested
2	Receive submission for an application for orphan medicinal product designation
3	Validate submission and assign rapporteurs
4	Start evaluation by drafting the summary report
5	Perform internal review and prepare the presentation to COMP
6	Co-ordinate COMP assessment - Outcome 1: list of questions to sponsor – go to step 7 - Outcome 2: opinion – go to step 9
7	Send list of questions to sponsor - Receive withdrawal request – END - Receive reply to list of questions – go to step 8
8	Hold oral explanation
9	COMP Opinion - Outcome 1: Positive- go to step 10 - Outcome 2: Negative – send for internal legal and regulatory review - go to step 11
10	Send COMP positive opinion and summary report to sponsor, and to the EC for decision
11	Send COMP negative opinion and summary report to sponsor; explain timelines for appeal
12	If appeal received, assign new rapporteurs, and go back to step 8
13	Send final COMP opinion and summary report after appeal to sponsor, and to the EC for decision
14	Publication of public summary of opinion - END

9.1.1 Process Flow Chart

Process map 1 - Procedure for orphan medicinal product designation and amendment of an existing orphan medicinal product designation

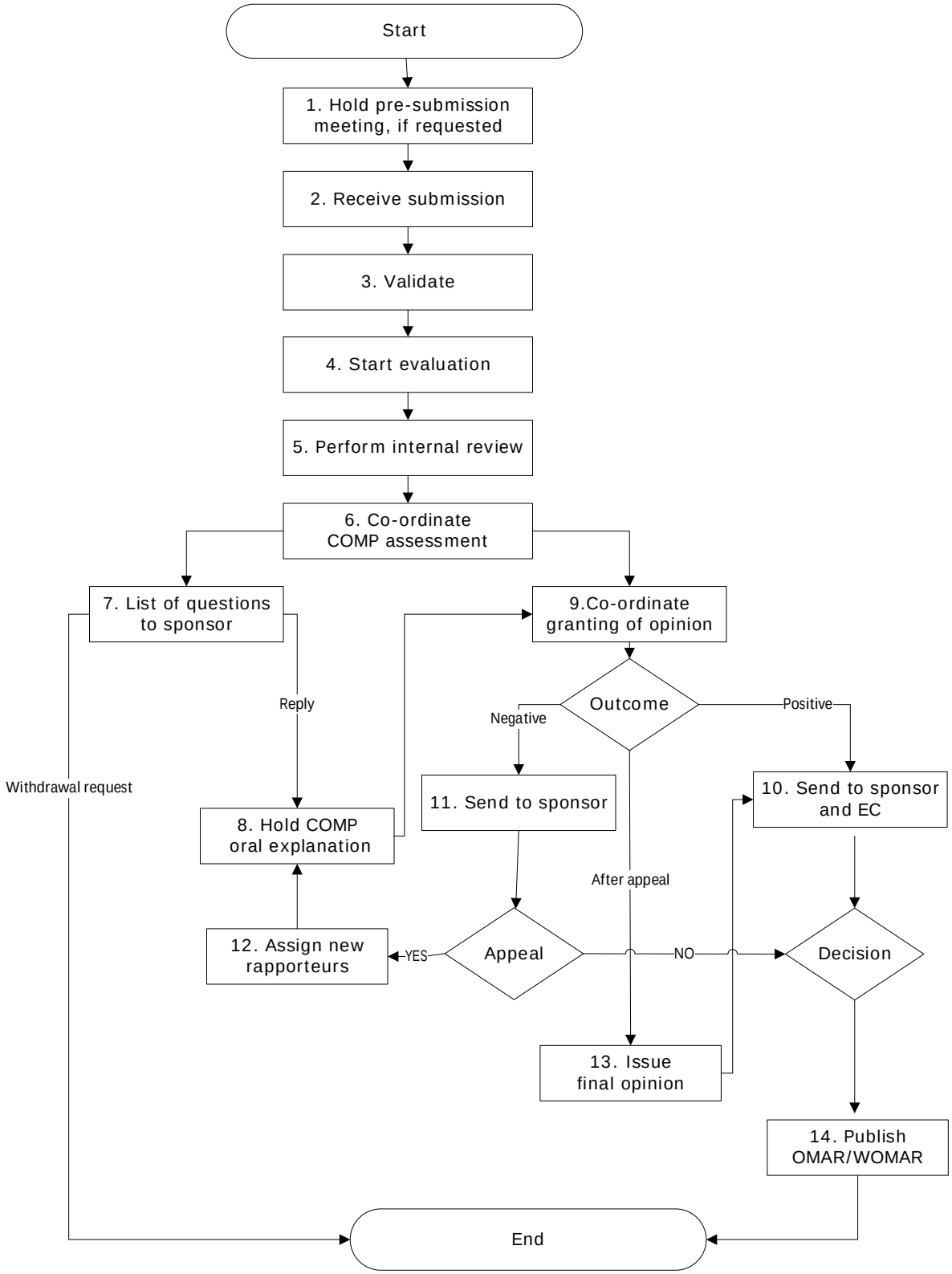


9.2 Procedure reviewing the orphan designation at the time of an initial application for marketing authorisation of an orphan medicinal product, or an extension of indication

Step	Action
1	Receive submission of maintenance report on the orphan drug designation criteria
2	Hold pre-assessment meeting, if requested
3	Assign rapporteurs
4	Start evaluation by drafting the summary report
5	Perform internal review and prepare the presentation to COMP
6	Co-ordinate COMP assessment - Outcome 1: list of questions to sponsor – go to step 7 - Outcome 2: opinion – go to step 9
7	Send list of questions to sponsor - Receive removal of orphan status request – END - Receive reply to list of questions – go to step 8
8	Hold oral explanation
9	COMP Opinion - Outcome 1: Positive – go to step 10 - Outcome 2: Negative – send for internal legal and regulatory review – go to step 11
10	Send COMP positive opinion and report on the review to sponsor, and to the EC for decision – go to step 14
11	Send COMP negative opinion and report on the review to sponsor; explain timelines for appeal
12	If appeal received, assign new rapporteurs, and go back to step 8
13	Send final COMP opinion and report on the review after appeal to sponsor, and to the EC for decision
14	Publish OMAR or WOMAR - END

9.2.1 Process Flow Chart

Process map 2 - Reviewing the orphan designation at the time of an initial application for marketing authorisation of an orphan medicinal product, or an extension of indication



9.3 Procedure for the review of the market exclusivity period of orphan medicinal products

Step	Action
1	Receive written justification from Member State that at least one of designation criteria of the orphan medicinal product may no longer be met
2	Ensure that the request can be addresed within the legal timeframe and assign rapporteurs and experts as applicable
3	Prepare 90 day procedure timetable for start at forthcoming COMP meeting
4	Provide the reasons from the Member State for triggering Art. 8(2) and procedural timetable to the EC and MAH
5	Internal review, drafting of summary report and presentation
6	Hold teleconference with MAH, as necessary and implement their justification
7	Add topic to the COMP agenda for discussion and co-ordinate COMP assessment and oral explanation with MAH (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 list of questions during the same plenary meeting
8	Day 1 - start of procedure and adoption of COMP list of questions for Step 1 (review of initial designation criteria) and Step 2 (return on investment assessment). Send assessment report with list of questions to MAH including invitation to an oral explanation at day 60
9	Day 30 - preliminary COMP discussion as required
10	Day 60 - MAH oral explanation for Step 1 list of questions and adoption of positive opinion or, if applicable, discussion with MAH on Step 2.
11	COMP opinion - Outcome 1: Positive trend, go to step 12 - Outcome 2: Negative trend, go to step 14
12	Send adopted COMP positive opinion and assessment report to MAH and to the EC, for decision
13	Publication of OMAR or WOMAR- END
14	Day 90 - 2nd MAH oral explanation for Step 2, adoption of COMP opinion Outcome 1: Positive – revert to step 12 Outcome 2: Negative – send for internal legal and regulatory review

Step	Action
15	Send COMP negative opinion and summary report to MAH; explain timelines for appeal and oral explanation
16	If appeal received, assign new rapporteurs, return to step 10
17	Send final COMP opinion to sponsor and to the EC for decision - return to step 13 - END

9.3.1 Process Flow Chart

Process map 3 - Procedure for the review of the market exclusivity period of orphan medicinal products.