



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Human Medicines Development and Evaluation

## Practical information for sponsors during the early phase of an orphan drug application

This is a short list of practical issues and information for sponsors planning to submit an application for designation of a medicine as an orphan medicinal product. It does not replace the legal requirements as set in the EU Directives, nor the guidelines available on the Agency website. The information is based on issues that frequently arise during the early phases of the application process, and is loosely organised as a simple list of issues.

### 1. Pre-submission meetings

The Agency strongly encourages sponsors to request a pre-submission meeting prior to filing an application for orphan medicinal product designation. Where possible, sponsors should request to the Agency a pre-submission meeting at least two months in advance prior to filing. Pre-submission meetings for orphan designation are free of charge.

The evaluation process has a fixed duration (90 days) and cannot be lengthened to accommodate for the lack of data or other omissions in the application submitted by the sponsor. For this reason, pre-submission meetings are advisable, as experience has shown that they have a positive impact on the success rate of the applications.

Pre-submission meetings will take place mostly via teleconference, unless the sponsor has a strong preference to come to the Agency in person. Our experience has shown that pre-submission meetings via teleconference are highly appreciated by sponsors, who do not need to worry about travel arrangements and the related expenses and the quality of the meeting is equivalent. Follow-up teleconferences are also possible.

Sponsors will be invited to take minutes of the meeting, which should be provided to the Agency within two weeks after the meeting. The Agency will subsequently review the minutes within 2 weeks, and agree the final (amended) minutes with the applicant.

Sponsors are strongly advised to use the common application form with the FDA available on the website to apply for orphan designation

[http://www.ema.europa.eu/pdfs/human/comp/EMEAFDA\\_Application\\_Form\\_for\\_Orphan\\_Medicinal\\_Product\\_Designation.doc](http://www.ema.europa.eu/pdfs/human/comp/EMEAFDA_Application_Form_for_Orphan_Medicinal_Product_Designation.doc).



If an application has not been submitted before to the FDA, the Agency encourages the sponsor to seek orphan designation from the FDA in the context of their collaboration. The Agency believes this is in the benefit of the development of orphan drugs for rare diseases.

### **Steps of the procedure**

On receipt of the sponsor's request the Agency will send the invitation to the pre-submission meeting or teleconference by e-mail. The sponsor will be requested to send to the Agency the following documentation electronically, at least one week in advance. At this stage the sponsor is recommended to use the secure e-mail system, Eudralink. Please contact the Eudralink Helpdesk at the Agency to open an account [eudralink@ema.europa.eu](mailto:eudralink@ema.europa.eu):

- a draft of the application (including application form and scientific part, but not the single PDF files for the references);
- a list of questions;
- a short power point presentation about the application (approx. 15 min, including condition, product and development stage);
- a list of participants;
- dial-in number and password for teleconference.

## **2. Format of the final application at the time of submission**

### **Electronic submission of applications for orphan designation**

Starting with the 18th February 2010 submission deadline, the European Medicines Agency will accept **electronic-only** orphan drugs applications for designation. This also applies to any responses to validation issues. Applicants should submit their applications on a CD or DVD with a cover letter. As previously, the deadlines for submission available on the Agency's website refer to the last acceptable day of receipt of electronic documentation.

For any questions please e-mail [orphandrugs@ema.europa.eu](mailto:orphandrugs@ema.europa.eu).

To minimise the amount of paper received, the applicant is also invited to send to the Agency any other documentation at any time during the procedure only by e-mail or using the secure e-mail system, Eudralink.

### **Documentation to be provided for the submission of an orphan drug application for designation by electronic means:**

The applicant shall submit to the Agency in electronic form the complete application for orphan drug designation including full copies of literature references. In parallel, the applicant should also submit the complete application directly to the address of the appointed COMP co-ordinator(s) [http://www.ema.europa.eu/htms/general/contacts/COMP/COMP\\_members.html](http://www.ema.europa.eu/htms/general/contacts/COMP/COMP_members.html).

Each of the submissions, to the Agency and to the COMP Co-ordinator(s) appointed, should include **signed paper copy of a cover letter** and a CD or a DVD, containing:

<b>Documentation</b>	<b>Format</b>
Cover letter	PDF
Application form. The application should be signed by no other than the sponsor. Useful links: European Medicines Agency application form <a href="http://www.ema.europa.eu/pdfs/human/comp/628300an.doc">http://www.ema.europa.eu/pdfs/human/comp/628300an.doc</a> Common European Medicines Agency/FDA application form <a href="http://www.ema.europa.eu/pdfs/human/comp/EMEAFDA_Application_Form_for_Orphan_Medicinal_Product_Designation.doc">http://www.ema.europa.eu/pdfs/human/comp/EMEAFDA_Application_Form_for_Orphan_Medicinal_Product_Designation.doc</a>	Word and signed PDF
Sections A-E of the application. Useful links: Guideline <a href="http://www.ema.europa.eu/pdfs/human/comp/628300en.pdf">http://www.ema.europa.eu/pdfs/human/comp/628300en.pdf</a>	Word
Proof of establishment of the sponsor in the EU	PDF
If applicable, letter of authorisation from the sponsor for the person/company acting on their behalf during the procedure	PDF
Translations of the name of the product and the proposed orphan indication into the official languages of the European Union, plus Icelandic and Norwegian <a href="http://www.ema.europa.eu/pdfs/human/comp/translation_table.doc">http://www.ema.europa.eu/pdfs/human/comp/translation_table.doc</a>	Word
Bibliography saved as single publications and titled as first author and year, such as in 'Smith PH et al 2004.PDF'.	PDF

### **Important**

If more than one indication is applied for the same product, separate applications should be submitted for each orphan indication. In this regard, 'treatment' and 'prevention' of the same condition are considered as two separate indications and should be the subject of two separate applications for orphan designation.

### **3. General advice**

- The name of a contact person at the sponsor's address in the European Economic Area must be provided; also please note that a P.O. box address is not acceptable.
- When selecting options in section I.2.2 (pages 4 and 5) of the application, sponsor should note that only one of three choices can be selected, as they are mutually exclusive; likewise, either option 2 or option 3 in section D (page 10) should be ticked.
- When considering the second option ("Other methods exist but are not considered satisfactory") in the above mentioned sections, sponsors should note that the existence of authorised medicines for the condition (or for a broader indication which includes the condition) excludes by default this

possibility, since an authorised medicine is automatically assumed to have a favourable risk/benefit ratio, and thus to be satisfactory. This is true even if improvements are always possible in medicine. Thus, if there are authorized medicinal products for the condition, “significant benefit” (third option) should be claimed and adequately justified.

- To use the secure e-mail system, Eudralink, please contact the Eudralink Helpdesk at the Agency to open an account [eudralink@ema.europa.eu](mailto:eudralink@ema.europa.eu).
- Sponsors are invited to consider the benefits of obtaining Small or Medium Enterprise status, if applicable; more information is available at <http://www.ema.europa.eu/SME/SMEoverview.htm>.
- For more detailed information on the submission of orphan drug applications, please refer to the Agency website at <http://www.ema.europa.eu/htms/human/orphans/guidance.htm>. In particular, the following documentation is available:
  - General information for Sponsors of Orphan Medicinal Products: <http://www.ema.europa.eu/pdfs/human/comp/479500en.pdf>
  - Guideline on the Format and Content of Applications for designation as Orphan Medicinal Products: <http://www.ema.europa.eu/pdfs/human/comp/628300en.pdf>
  - Annex to guideline on the format and content of applications for designation as orphan medicinal products: <http://www.ema.europa.eu/pdfs/human/comp/628300an.doc>
  - European Medicines Agency/FDA common application form: [http://www.ema.europa.eu/pdfs/human/comp/EMEAFDA\\_Application\\_Form\\_for\\_Orphan\\_Medicinal\\_Product\\_Designation.doc](http://www.ema.europa.eu/pdfs/human/comp/EMEAFDA_Application_Form_for_Orphan_Medicinal_Product_Designation.doc)
  - Points to Consider on the Calculation and Reporting of the Prevalence of a Condition for Orphan Designation: <http://www.ema.europa.eu/pdfs/human/comp/043601.pdf>
  - Draft Guideline on Elements required to Support the Medical Plausibility and the Assumption of Significant Benefit for an Orphan Designation: <http://www.ema.europa.eu/pdfs/human/comp/1589309en.pdf>

For any other question, sponsors are welcome to contact the Agency staff directly.