Department of Health and Human Services
Food and Drug Administration

COMMON EMEA / FDA APPLICATION FOR ORPHAN MEDICINAL PRODUCT DESIGNATION

Form Approved

OMB Control Number: 0910-0167
Expiration Date: December 31, 2017

See OMB Statement on final page.

The sponsor of a medicinal product[1] for human use may desire to seek orphan designation of its medicinal product for use to diagnose, treat, or prevent a rare disease or condition from the European Commission in accordance with Regulation (EC) No 141/2000 of 16 December 1999 and Commission Regulation (EC) No 847/2000, and from the United States Food and Drug Administration (FDA) in accordance with section 526 of the Federal Food, Drug, and Cosmetic Act (FDCA) (21 U.S.C. 360bb). In such case, the sponsor may apply for orphan designation of the same medicinal product for the same use in both jurisdictions by using this common application form for its submissions to the European Medicines Agency (EMEA) and the FDA.

The application may be submitted to the European Medicines Agency (EMEA)[2] and to the FDA Office of Orphan Products Development.[3]

Note: The sponsor should consult the "Guideline for the format and content of applications for designation as orphan medicinal products" (ENTR/6283/00) when completing the application to EMEA. Relevant sections defined in this Guideline must be submitted to EMEA. An application[4] submitted to FDA must comply with 21 U.S.C. 360bb and 21 CFR Part 316 et seq., irrespective of whether this form is used.

The sponsor must submit one original copy in paper (signed and dated) and two electronic copies to EMEA. FDA requires either two paper copies of the application or it may be submitted via electronic format through the use of physical media (see "Draft Guidance for Industry: Providing Regulatory Submissions in Electronic Format for Orphan Drug and Humanitarian Use Device Designation Requests and Related Submissions").[5]

THIS APPLICATION CONCERNS *(Please check the appropriate item.)*

- ☐ **An active substance not currently authorised**[6,7]
- ☐ **An active substance currently authorised for another indication**
- ☐ **A potentially clinically superior medicinal product containing the same active substance as one in an already authorised medicinal product for the same orphan use (for application to FDA only)**

Note: The sponsor may apply for orphan designation of a previously unapproved medicinal product, or an already authorised medicinal product for a new orphan indication. The sponsor may also seek and obtain orphan designation of a medicinal product containing the same active substance as one in an already authorised medicinal product from FDA, if it can present a plausible hypothesis of clinical superiority. The sponsor must append information to support such hypothesis to this application.[8] In the application to EMEA if the sponsor is the holder of an existing marketing authorisation in the European Community for this product, the sponsor should provide details of the currently authorised indication(s) and the type of marketing authorisation granted.

(Note continued, page 2)

1 The term "medicinal product" is used in this document in place of the word "drug" used in the FDA Orphan Drug Regulations (21 CFR Part 316) without any intention to alter its regulatory meaning.

2 See http://www.emea.europa.eu/

3 See http://www.fda.gov/orphan/

4 The word "application" is used in this document in place of the word "request" used in the FDA Orphan Drug Regulations without any intention to alter its regulatory meaning.

5 See http://www.fda.gov/orphan/esub/esub.htm

6 The term "active substance" is used in this document in place of the term "active moiety" (if the medicinal product is a small molecule), and "principal molecular structural features" (if the medicinal product is a large molecule) as used in the FDA Orphan Drug Regulations without any intention to alter their regulatory meaning.

7 The word "authorised" is used in this document in place of the word "approved" used in the FDA Orphan Drug Regulations without any intention to alter its regulatory meaning.

8 See §§ 316.20(a) and 316.20(b)(5) for application to FDA.

(Continued)

The application for orphan designation must be submitted prior to the submission of a marketing authorisation application of the medicinal product for the orphan indication.[9]

The sponsor must comply with Guideline ENTR/6283/00 (application to EMEA), and 21 CFR §§ 316.20(a) and 316.23 (application to FDA) when completing this section.

REQUIRED INFORMATION FOR DESIGNATION

1) This application is submitted in accordance with the following provision of Article 3(1)(a), Regulation (EC) 141/2000, or Section 526 of the FDCA *(Please check the appropriate item.)*

☐ Prevalence of a disease or condition below the statutory threshold

Note: The sponsor must append documentation, with authoritative references, to demonstrate that the number of people affected by the disease or condition in the European Union (application to EMEA), or United States (application to FDA) meets the respective statutory prevalence threshold. The sponsor must include a description of the methodology used for gathering the data, data sources (including dates of information provided and literature sources), calculations, and results of these calculations.[10]

The sponsor must comply with section B on "Prevalence of the condition" of Guideline ENTR/6283/00 (application to EMEA), and 21 CFR §§ 316.20(b) and 316.21 (application to FDA) when completing this section.

☐ Potential for lack of return on investment/no reasonable expectation of cost recovery

Note: The sponsor must append documentation, with authoritative references, to demonstrate that, without incentives, there is no reasonable expectation that costs of research and development of the medicinal product for the orphan indication can be recovered if the medicinal product is authorised for marketing in the European Community (application to EMEA) or in the United States (application to FDA).[11] For application to EMEA, the sponsor should also include information showing it is unlikely that the marketing of the medicinal product in the European Community would generate sufficient return to justify the necessary investment.

The sponsor must comply with section C on "Potential for return on investment" of Guideline ENTR/6283/00 (application to EMEA), and 21 CFR §§ 316.20(b), 316.21(c) and (d) (application to FDA) when completing this section.

2) Name of the Active Substance(s):

[9] See § 316.23(a) for application to FDA. See also § "Timing for submission" of Guideline ENTR/6283/00 for application to EMEA.

[10] See §§ 316.20(b)(8) and 316.21(b) for application to FDA. See also § B of Guideline ENTR/6283/00 and Points to consider COMP/436/01 for application to EMEA.

[11] See §§ 316.20(b)(8)(ii), 316.21(c) and (d) for application to FDA. See also § C of Guideline ENTR/6283/00 for application to EMEA.

Note: In the application to EMEA, the sponsor should indicate whether the name provided is the proposed/accepted International Nonproprietary Name, European Pharmacopoeia name, National Pharmacopoeia, official compendia name, common name, or scientific name. In the application to FDA, the sponsor should provide the generic name (such as the United States Adopted Name Council-approved name) and trade name, if any, of the medicinal product.[12]

The proposed/accepted trade name in the European Community, the Anatomical Therapeutic Chemical code, the proposed strength, pharmaceutical form, and route of administration for the medicinal product, if available, should also be included in the application to EMEA, but they are not required in the application to FDA (see 21 CFR § 316.20(b)).

3) Proposed Orphan Designation

Note: The sponsor must append a description of the rare disease or condition for which the medicinal product is being or will be investigated, and the reasons why such therapy is needed.[13] If more than one designation is applied for, the sponsor should submit a separate application for each designation (e.g., one application for the treatment indication and one application for the prevention indication of the medicinal product for the rare disease or condition). If the medicinal product is under development for only a subset of persons with a disease or condition, the sponsor must demonstrate the medical plausibility why the remaining persons with the same disease or condition are not appropriate candidates for use of the medicinal product.[14]

The sponsor must also append a discussion on the rationale for the use of the medicinal product for the rare disease or condition in question. All relevant supportive information from non-clinical studies, clinical investigations, and other evidence available to the sponsor, whether positive, negative, or inconclusive, must be submitted.[15]

The sponsor must comply with section A on “Description of the condition” of Guideline ENTR/6283/00 (application to EMEA), and 21 CFR § 316.20(b) (application to FDA) when completing this section.

4) Summary of Development Status and Regulatory History

Note: The sponsor must append a summary of the world-wide regulatory status and marketing history of the medicinal product to include, where applicable, current investigational uses, previous marketing approvals, orphan status, and adverse regulatory actions, if any, in any country.[16]

The sponsor must comply with section E on "Description of the stage of development" of Guideline ENTR/6283/00 (application to EMEA), and 21 CFR § 316.20(b)(7) (application to FDA) when completing this section.

[12] See § 316.20(b)(2) for application to FDA.

[13] See § 316.20(b)(3) for application to FDA.

[14] See § 316.20(b)(6) for application to FDA. See also § A3 of Guideline ENTR/6283/00 for application to EMEA.

[15] See § 316.20(b)(4) for application to FDA. See also § A3 of Guideline ENTR/6283/00 for application to EMEA.

[16] See § 316.20(b)(7) for application to FDA. See also § E of Guideline ENTR/6283/00 for application to EMEA.

5) Information on the Sponsor

NAME / CORPORATE NAME

CONTACT PERSON / TITLE

ADDRESS	TELEPHONE
	TELEFAX
	E-MAIL
COUNTRY	

Note: In the application to FDA, information on telefax and e-mail is optional.

6) Information on the entity authorised for communication on behalf of the sponsor *(if different from section 5)*

NAME / CORPORATE NAME

CONTACT PERSON / TITLE

ADDRESS	TELEPHONE
	TELEFAX
	E-MAIL
COUNTRY	

Note: The sponsor should append a letter authorising the named entity to communicate on behalf of the sponsor, if applicable. Please note that in the application to EMEA, for sponsors whose main business is operated from outside the European Economic Area (EEA) an EEA-established person, or a company, as a contact person for communication should be provided. A proof of establishment in the EEA should be provided in any case. In the application to FDA, a non-United States sponsor must name a permanent resident in the United States as the sponsor's agent together with his/her address, through whom all communications will be made on behalf of the sponsor as required in 21 CFR § 316.22.

7) Information on the manufacturer(s)

a) Manufacturer(s) and site(s) of manufacture of the active substance(s):

NAME / CORPORATE NAME

CONTACT PERSON / TITLE

ADDRESS	TELEPHONE
	TELEFAX
	E-MAIL
COUNTRY	

b) Manufacturer(s) and site(s) of manufacture of the finished medicinal product:

NAME / CORPORATE NAME

CONTACT PERSON / TITLE

ADDRESS	TELEPHONE
	TELEFAX
	E-MAIL
COUNTRY	

Note: For products that are in the early stages of development it may not be possible to provide the above information. In application to FDA, only the name and address of the source of the active substance is required, if it is not manufactured by the sponsor.[17]

[17] See § 316.20(b)(2) for application to FDA.

ADDITIONAL REQUIREMENTS EXCLUSIVE TO APPLICATION TO EMEA

1) If the active substance scope of the application is authorised in the European Union *(Please check the appropriate item.)*

☐ a) Centralised authorisation (in accordance with Regulation (EC) No 726/2004)

TRADE NAME

DATE OF AUTHORISATION *(mm/dd/yyyy)*

MARKETING AUTHORISATION NUMBER(S)

MARKETING AUTHORISATION HOLDER

☐ b) Mutual recognition (in accordance with Article 28 of Directive 2001/83/EC)

REFERENCE MEMBER STATE

DATE OF AUTHORISATION *(mm/dd/yyyy)*

MARKETING AUTHORISATION HOLDER

CONCERNED MEMBER STATE(S) *(Please check applicable.)*

☐ AT	☐ BE	☐ BG	☐ CY	☐ CZ	☐ DE	☐ DK	☐ EE	☐ EL	☐ ES
☐ FI	☐ FR	☐ HU	☐ IS	☐ IE	☐ IT	☐ LI	☐ LT	☐ LU	☐ LV
☐ MT	☐ NL	☐ NO	☐ PL	☐ PT	☐ RO	☐ SE	☐ SI	☐ SK	☐ UK

Note: Please attach details of trade name(s) and marketing authorisation number(s).

☐ c) National procedure

DATE OF AUTHORISATION *(mm/dd/yyyy)*

MARKETING AUTHORISATION HOLDER

MEMBER STATE(S) WHERE AUTHORISED *(Please check applicable.)*

☐ AT	☐ BE	☐ BG	☐ CY	☐ CZ	☐ DE	☐ DK	☐ EE	☐ EL	☐ ES
☐ FI	☐ FR	☐ HU	☐ IS	☐ IE	☐ IT	☐ LI	☐ LT	☐ LU	☐ LV
☐ MT	☐ NL	☐ NO	☐ PL	☐ PT	☐ RO	☐ SE	☐ SI	☐ SK	☐ UK

Note: Please attach details of trade name(s) and marketing authorisation number(s).

2) Article 3(1)(b), Existence of Other Methods of Diagnosis, Prevention or Treatment *(Please check the appropriate item.)*

☐ No other methods exist in the community

Note: For the documentation submitted in support of this application, section D(1) of Guideline ENTR/6283/00 should contain a statement that no other methods currently exist.

☐ Other methods exist but are not considered satisfactory

Note: For the documentation submitted in support of this application, sections D(1) and D(2) of Guideline ENTR/6283/00 should be completed.

☐ Other satisfactory methods exist but this medicinal product will be of significant benefit to those affected by the condition

Note: For the documentation submitted in support of this application, sections D(1) and D(3) of Guideline ENTR/6283/00 should be completed.

3) Attach proof of establishment of the sponsor in the European Economic Area.

4) Information on the sponsor whose main business is outside the European Community

NAME / CORPORATE NAME

CONTACT PERSON / TITLE

ADDRESS	TELEPHONE
	TELEFAX
	E-MAIL
COUNTRY	

5) Other Information

a) Scientific advice

HAS SCIENTIFIC ADVICE BEEN GIVEN BY THE CHMP FOR THIS MEDICINAL PRODUCT?

☐ Yes ☐ No

IF YES, PLEASE PROVIDE DATE OF THE SCIENTIFIC ADVICE MEETING *(mm/dd/yyyy)*	REFERENCE OF THE SCIENTIFIC ADVICE LETTER

Note: Please append a copy of the scientific advice letter.

b) Protocol assistance

DO YOU INTEND TO SEEK PROTOCOL ASSISTANCE FOR THIS MEDICINAL PRODUCT?

☐ Yes ☐ No

IF YES, PLEASE PROVIDE THE PROJECTED DATE

c) Application for marketing authorisation

PLEASE PROVIDE DETAILS ON THE PLANNED SUBMISSION OF THE MARKETING AUTHORISATION APPLICATION FOR THE ORPHAN INDICATION, IF KNOWN.

DO YOU INTEND TO REQUEST A FEE REDUCTION?

☐ Yes ☐ No

6) Information on the entity responsible for research and development of the medicinal product *(if different from section 5 of the Required Information for Designation above)*

NAME / CORPORATE NAME

CONTACT PERSON / TITLE

ADDRESS	TELEPHONE
	TELEFAX
	E-MAIL
COUNTRY	

ADDITIONAL REQUIREMENT EXCLUSIVE TO APPLICATION TO FDA

Statement of Party of Interest *(See note below.)*

Note: The sponsor must state whether it is the real party in interest of the development, production, and sales of the orphan medicinal product as required in 21 CFR § 316.20(b)(9).

DECLARATION AND SIGNATURE

NAME OF THE MEDICINAL PRODUCT(S) / ACTIVE SUBSTANCE(S)

PROPOSED ORPHAN DESIGNATION (I.E., DIAGNOSIS, TREATMENT, OR PREVENTION OF A RARE DISEASE OR CONDITION)

SPONSOR

The above named sponsor hereby requests orphan designation for the above named medicinal product for the above named indication.

It is hereby confirmed that all relevant information required for the orphan designation of this medicinal product has been included in the application. It is hereby confirmed also that the information provided in the application is complete and accurate to the best of the sponsor's knowledge.

SPONSOR – Signature	Place
Title	Date *(mm/dd/yyyy)*

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 32 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

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