30.09.2013

# Submission of comments on ' Guideline on the format and content of applications for designation as orphan medicinal products and on the transfer of designations from one sponsor to another ' (ENTR/6283/00 Rev 4)

## Comments from:

| Name of organisation or individual |
| --- |
| Novartis Pharma AG |

## 1. Specific comments on text

| Line number(s) of the relevant text | Comment and rationale; proposed changes |
|---|---|
| | Novartis welcomes the possibility to comment on the draft "Guideline on the format and content of applications for designation as orphan medicinal products and on the transfer of designations from one sponsor to another". The draft guideline is useful as it provides further clarity to the sponsor on how to handle orphan designation applications. |
| | Novartis notes that there are discrepancies between the content of the guidance and that of the application form, and these discrepancies are highlighted in these comments. |
| Section "Documentation to be supplied", p. 5 | Comment: The draft guideline suggests that "The application should contain about 30 pages." Novartis recommends that this text is aligned with the guidance given for the Clinical Overview in the Notice to Applicants, since there is no need to strive for 30 pages if a shorter document is feasible.<br>Proposed change (if any):"The application should ***generally be a relatively short document*** (about 30 pages)." |
| Section "Documentation to be supplied", p. 5 | Comment: In the draft guideline it is suggested that "A sponsor shall submit to the EMA an electronic version of the complete application for designation including full bibliographical references to orphandrugs@ema.europa.eu ." Novartis proposes that the guideline also mentions the deadlines for submission.<br><br>Proposed change (if any): "A sponsor shall submit to the EMA an electronic version of the complete application for designation including full bibliographical references to orphandrugs@ema.europa.eu ***and in accordance with published deadlines for submission, available on the EMA website***". |
| Section "Information to be included in the application form (Annex)", p. 6 | Comment: Novartis notes that a new field has been added for the "Unified Product Identifier number (UPI)" on the cover page of the draft application form. Novartis believes that a reference to or definition of this should be included in this section. |
| Section "5 Manufacturers ", p. 6 | Comment: Novartis notes that the draft application form no longer refers to the active substance manufacturer. If the details of the active substance manufacturer are no longer required, this section should be changed accordingly. |
| Section "1. Details of the condition", p. 6 | Comment: The draft guideline suggests that "When applicable, this section should refer to the condition according to International disease classification system such as ICD and other well recognised systems". Novartis believes that the |

| Line number(s) of the relevant text | Comment and rationale; proposed changes |
|---|---|
| | current wording of the sentence is confusing as it implies that all the classification systems should be used and therefore suggests that "and" is changed to "or".<br><br>Proposed change (if any): "When applicable, this section should refer to the condition according to International disease classification system such as ICD **or** other well recognised systems." |
| Section "2. Proposed therapeutic indication", p. 6 | Comment: In the draft guideline it is proposed that the header of this section is changed from "Proposed orphan indication" to "Proposed therapeutic indication". Novartis believes that the changed section header does not match the section content since the concept of orphan indication is broader than the concept of therapeutic indication. The therapeutic indication may also change over the course of drug development. Therefore, Novartis proposes to keep the section header unchanged. |
| Section "3. Medical Plausibility", p. 7 | Comment: It is proposed that "All available studies should be submitted at the time of the application." Novartis assumes that this sentence refers only to the studies mentioned in the preceding sentence (e.g. related to the specific condition and patient population). Therefore, Novartis recommends that "all available studies" and "at the time of the application" are better defined.<br><br>Proposed change (if any): "***Where available, reports of studies relevant to the specific condition should be included with the orphan designation application***". |
| Section "B prevalence of the condition", p .8 | Comment: Novartis notes that the draft application form still contains information about section B3 "Information on participation in other Community projects". However, this section has been deleted in the draft guideline. Novartis requests clarification on whether section B.3 is still required. If the section is no longer required then the draft application form should be amended accordingly. |
| Section "D 2. Justification as to why methods are not satisfactory", p. 12 | Comment: In the revised guideline there is a deletion of the clarification that either section D2 or section D3 is completed, but not both. Novartis believes that the clarification that was available by so far is useful and should be maintained, even though there is a general guidance provided earlier in the document ("D2 and D3 are mutually exclusive and only one of them should be filled in"). |
| Section "D 3. Justification of significant benefit" p. 12 | Comment: In the draft guideline it is mentioned that "serious and documented difficulties with the formulation or route of administration or compliance" should be discussed. Novartis believes that the term "serious and documented difficulties with the formulation" is not sufficiently well defined, especially since the reference to "compliance-promoting |

| Line number(s) of the relevant text | Comment and rationale; proposed changes |
|---|---|
| | features or evidence to show fewer interactions with food or other medicinal products" is proposed for deletion. In order to improve clarity Novartis suggests to maintain the reference to interactions, and to include improvement of the quality of life (in line with EMA/COMP/15893/2009).<br><br>Proposed change (if any): "…this should be accompanied by a discussion on serious and documented difficulties with the formulation ***(such as interactions with food or other medicinal products)*** or route of administration or compliance. ***Other arguments that may improve the quality of life of the patients may also be considered for this purpose***." |
| Section "D 3. Justification of significant benefit" p. 13 | Comment: Novartis believes that in order to improve the clarity in the two paragraphs talking about orphan designation review at the time on marketing authorisation application and orphan designation after CHMP opinion should be presented in reverse order.<br><br>Proposed change (if any): "At the time the application for marketing authorisation is reviewed, sponsors of designated orphan medicinal products will be required to demonstrate significant benefit over currently authorised methods in order to maintain orphan status. At this stage, the COMP will require a higher level of data/evidence for the orphan status than at the time of designation to be maintained.<br>***All designations based on the significant benefit criterion will be reviewed prior to the grant of a marketing authorization and after adoption of the opinion by the CHMP.***" |
| Application form, p. 7 | Comment: the introduction to section II.5 refers to section II.5.2, however, this sub-heading does not exist anymore. |