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EMA/COMP/150409/2006 Rev.1[1]
Human Medicines

COMP members interaction with sponsors of orphan designation applications[2]

This document addresses the COMP - sponsor interface and the involvement of EMA staff in such interaction.

1. Transparency/Declaration of Interests[3]/Code of Conduct[4]

The membership of the COMP is made public. When each new appointment is published the professional qualifications of each COMP member is specified.

COMP members and their experts are bound by the EMA's Code of Conduct, which addresses personnel behavioural aspects such as confidentiality and discretion, directions on invitations and gifts and declarations of conflicts of interest. As regards the latter it should be noted that COMP members or their experts may not have financial or other interests in the pharmaceutical industry, which could affect their impartiality. All indirect interests, which could relate to the pharmaceutical industry, are entered through an annually updated Declaration of Interests (DoI) in a register which is held by EMA and which the public may consult. In addition, a copy of each member's DoI is available to the public via the EMA's website.

Members should declare at the start of each plenary meeting or supporting meeting any specific interests considered prejudicial to their independence with respect to specific points on the agenda.

[1] General formatting, links added, header and footer updated, wording revised, new procedures listed under heading 4.7.

[2] This document applies to the following procedures involving the COMP assessment: orphan designation, orphan designation amendment, orphan designation maintenance, review of the period of market exclusivity of orphan medicinal products.

[3] European Medicines Agency policy on the handling of competing interests of scientific committees' members and experts.

[4] EMA Code of Conduct.
Appendix to EMA Code of Conduct.

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2. Overview of procedure for orphan designation

Sponsors submit orphan designation applications via the IRIS portal. The applications are available to all COMP members. For each application one COMP rapporteur and one EMA co-ordinator are appointed.

The EMA co-ordinator is responsible for validating the application. In the event that additional data, information or clarification is required to complete the validation, the sponsor is contacted in writing and asked to respond within 60 days. Once the validation process is successfully completed, the evaluation timetable starts and EMA sends a listing of all applications starting the evaluation process to all COMP members.

During the evaluation phase the EMA co-ordinator, in association with the COMP rapporteur, drafts a summary report on the application which is available to all COMP members for comments prior to the first discussion at Committee level. Where there is a need for written/oral explanation from the sponsor, the COMP rapporteur and the EMA co-ordinator draft a list of issues for adoption by the Committee. Before day 90, the COMP adopts its opinion.

In case of a negative opinion, the sponsor may appeal. The COMP will appoint a different COMP rapporteur for the appeal, the EMA co-ordinator generally remains the same. The grounds for appeal are submitted by the sponsor within 90 days following its receipt of the opinion. The summary report will be revised to reflect the submitted appeal. The COMP will consider whether its opinion should be revised at the first meeting following receipt of the grounds for appeal.

EMA forwards the final opinion to the sponsor and to the European Commission (EC) for the decision-making process.

3. Interaction with sponsors

Sponsors considering submission of an orphan designation application may informally liaise with any member of the COMP or the Orphan Medicines Office of EMA, prior to formally submitting the application.

3.1. Appointment of rapporteurs

Following receipt of an application, a COMP rapporteur will be appointed by the COMP. The rapporteur shouldn't have any prior or current relationship with the sponsor that might be perceived as a potential conflict of interest. Involvement with the sponsor on behalf of a national competent authority would not normally be considered to represent a conflict of interest. However, it would not be acceptable for a rapporteur to have previously acted on behalf of the sponsor or to have been extensively involved in the product's development as an investigator or commercial consultant.

3.2. Pre-submission phase

Sponsors are strongly encouraged to request a pre-submission meeting/teleconference with EMA prior to filing, to discuss their draft application. The pre-submission phase is handled by EMA and, generally, the COMP members do not participate in pre-submission meetings. However, they can be consulted by EMA, if needed.

3.3. Validation phase

The EMA co-ordinator takes the lead during the validation phase where the application is checked for 'completeness' in accordance with the data requirements for a designation application. Although, the COMP rapporteur for the procedure may be already appointed, the sponsor should contact the EMA co-ordinator in relation to validation questions.

3.4. Evaluation phase (day 1-90)

During the evaluation phase, apart from the appointed COMP rapporteur, it is not considered appropriate for COMP members to have any contact with the sponsor in relation to the application.

The EMA co-ordinator or the COMP rapporteur may contact the sponsor when drafting the summary report should the need arise to clarify any aspect of the review. It is recommended that any written communication is exchanged via the IRIS case e-mail and that any information provided by the sponsor is uploaded in the relevant case folder via the IRIS portal.

The sponsor having received the formal COMP list of issues may seek clarification to prepare an adequate response package/oral explanation. Such requests are considered appropriate and the COMP rapporteur and EMA co-ordinator may provide additional information regarding the COMP discussion that led to the adoption of the list of issues to aid understanding of the questions and facilitate preparation of an adequate response by the sponsor. They may also discuss with the sponsor the broad outline of their response strategy including any amendment to the indication applied for. Such contacts should be documented, and any information provided by the sponsor should be available in the IRIS case.

During this period, it should be understood by the sponsor that any direct and individual contacts with COMP members other than the appointed COMP rapporteur are not considered appropriate and the COMP members should refer sponsors contacting them during the evaluation phase to the co-ordinators. Sometimes another COMP member may have specific clinical or other expertise that might be of value in assisting the sponsor to prepare an adequate response. In this event the other COMP member should provide advice to the co-ordinators and should not directly communicate with the sponsor.

Following the conclusion of an oral explanation, the COMP rapporteur and the EMA co-ordinator will debrief the sponsor and communicate the outcome of the COMP discussion, including the result of any trend vote where consensus has not been reached. In the event of a negative trend vote, the sponsor must be sufficiently informed via this debriefing to allow a decision to either withdraw the application or proceed to a negative opinion. In the event of a positive opinion, the sponsor must be informed of the final orphan indication considered acceptable by the Committee. If the COMP is aware of circumstances that might impact on the review of the designation criteria at the time of marketing authorisation, this information should also be communicated to the sponsor provided it does not involve the disclosure of confidential information.

3.5. Post-opinion

If the sponsor has comments relating to the final opinion adopted by the Committee these should be channelled through the EMA co-ordinator. Queries relating to the decision-making phase may be directed to the appropriate contact point within DG Health and Food Safety at the EC.

3.6. Contacts with COMP members during an appeal process

If the COMP opinion is appealed a new COMP rapporteur is appointed, the EMA co-ordinator will generally remain the same. Direct contact with the initial COMP rapporteur should cease as soon as the new rapporteur is appointed. Individual contacts with COMP members other than the appointed appeal rapporteur are not considered acceptable and COMP members are advised to reject such contacts. This must be particularly emphasised where the opinion under appeal has been adopted by majority and the divergent views of individual members is known as the sponsor may attempt to lobby those members directly.

3.7. Post-designation

Post-designation procedures involving the COMP assessment include:

- orphan designation amendment;

- orphan designation maintenance at the time of marketing authorisation;

- review of the period of market exclusivity of orphan medicinal products.

The sponsor should direct any queries related to the procedures to EMA. As mentioned previously, direct contact with COMP members other than the appointed rapporteur, is not considered appropriate.

The sponsor is required to submit an annual report on the state of development of designated medicinal products to EMA up until the first application for marketing authorisation, within the scope of the orphan condition, is submitted in the EU. The sponsor should direct any queries related to the designation, including any transfer of sponsorship or queries on annual report timing/preparation to EMA.