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COMP Members Interaction with Sponsors of Applications for Orphan Designation

I. Background

During the COMP audit (A04008) in September 2004 a questionnaire was circulated to COMP members to gather information on the organisation and functioning of the Committee and the nature of its external contacts. During this survey 50% of respondents indicated a need for guidance to govern contact with sponsors. The Audit report, therefore, contained an Opportunity for Improvement to prepare a procedure for COMP interaction with sponsors of applications for orphan designation. Accordingly, this document has been prepared to address the COMP-sponsor interface. The involvement of EMEA staff in such interaction will also be addressed.

II. Transparency/ /Declaration of Interests /Code of Conduct

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 EMEA's Code of Conduct¹, 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, who could relate to the pharmaceutical industry, are entered through an annually updated Declaration of Interests (DoI) in a register which is held by the Agency and which the public may consult. In addition a copy of each Member's DoI is now systematically made available to the public via the EMEA'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.

III. Overview of Procedure for Orphan Designation

Sponsors notify the EMEA of their intention to submit an application at the latest two months prior to the planned submission date. Two co-ordinators (1 COMP member, 1 EMEA staff member) are then appointed for each application prior to its submission.

Once submitted, the two co-ordinators are provided with copies of the application. The EMEA Secretariat is responsible for validating the application. In the event that the EMEA requires additional data, information or clarification to complete its validation, the sponsor is contacted in writing (with COMP co-ordinator on copy) and asked to respond within a 3-month time limit. Once the validation process is successfully completed, the evaluation time-table starts and the EMEA sends a copy of the application to all COMP members.

¹ DoI/Code of Conduct EMEA/H/31653 "EMEA Policy on the Handling of Conflicts of Interests for Committee Members and Experts"

During the evaluation phase the EMEA co-ordinator, in association with the COMP co-ordinator, drafts a summary report on the application which is circulated 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 Co-ordinators 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 co-ordinator for the appeal, the EMEA co-ordinator generally remains the same. The grounds for appeal are received from the sponsor within 90 days following its receipt of the opinion. The co-ordinators prepare a revised summary report on the appeal documentation. The COMP considers whether its opinion should be revised at the first meeting following receipt of the grounds for appeal.

The EMEA forwards the final opinion to the sponsor and to the Commission for the decision-making process.

IV. Interaction with sponsors

Sponsors considering submission of an application for orphan designation may informally liaise with any member the COMP or the Scientific Advice and Orphan Drugs Sector of the EMEA, prior to formally notifying their intent to submit the application.

- **Appointment of co-ordinators**

Upon receipt of notification of intent to file, a COMP co-ordinator and EMEA co-ordinator will be appointed for the upcoming application. Neither co-ordinator should 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 co-ordinator 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.

- **Pre-submission phase**

Once co-ordinators have been appointed for an upcoming application, sponsors should address any questions relating to the application for orphan designation to these persons. Contact should generally be channelled through the EMEA co-ordinator. Both co coordinators should be updated on any relevant contacts with the sponsor.

Sponsors are strongly encouraged to request a pre-submission meeting or teleconference with the EMEA prior to filing to discuss their draft application. Generally the COMP co-ordinator does not participate in the pre-submission meeting, however, if the sponsor has issues that it would like both co-ordinators to comment on, participation of the COMP co-ordinator, in person or via teleconference, can be organised.

- **Validation phase**

The EMEA co-ordinator takes the lead during the validation phase where the file is checked for 'completeness' in accordance with the data requirements for a designation application. Although, the COMP co-ordinator is kept informed of any validation issues arising, the sponsor should contact the EMEA co-ordinator in relation to validation questions.

- **Evaluation phase (day 1-90)**

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

The EMEA or COMP co-ordinator may contact the sponsor when drafting the summary report should the need arise to clarify any aspect of the review. It is recommended that such contacts are documented and that any information provided by the sponsor is copied to both co-ordinators.

The sponsor having received the formal COMP List of Issues may seek clarification from the co-ordinators to prepare an adequate response package/oral explanation. Such requests are considered appropriate and the co-ordinators 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. The co-ordinators 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 copied to both co-ordinators. If a meeting is organised to prepare the sponsor's response to the COMP List of Issues both coordinators should be involved.

During this period it should be understood by the sponsor that any direct and individual contacts with COMP members other than the appointed COMP co-ordinator are not considered appropriate and 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 particular 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 co-ordinators hold a debriefing meeting with the sponsor to 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.

- **Post-Opinion**

If a sponsor has comments relating to the final Opinion adopted by the Committee these should be channelled through the EMEA co-ordinator. Queries relating to the decision-making phase may be directed to the appropriate contact point within DG Enterprise at the European Commission.

- **Contacts with COMP members during an appeal process**

If a COMP opinion is appealed a new COMP co-ordinator is appointed, the EMEA co-ordinator will generally remain the same. Direct contact with the initial COMP co-ordinator should cease as soon as the new co-ordinator is appointed. Individual contacts with COMP members other than the appointed appeal co-ordinators 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.

- **Post-Designation**

The sponsor is required to submit an annual report on the state of development of designated medicinal products to the EMEA 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 maintenance of its designation, including any transfer of sponsorship or queries on annual report timing/preparation to its EMEA co-ordinator.

The sponsor is required to submit a report on significant benefit at the time the application for marketing authorisation is submitted. The sponsor should direct any queries related to the report on significant benefit of its designation to its EMEA co-ordinator.

Direct contact with COMP members to discuss maintenance of an existing orphan designation is not considered appropriate in the post designation phase.