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To: EO-PresubmissionConsultation
Cc: [redacted]
Subject: Comments Ombudsman Inquiry on EMA pre-submission activities
Attachments: AT-response to European Ombudsmans inquiry.docx

Follow Up Flag: Follow up
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Dear colleagues,

please find enclosed the answers from the Austrian Medicines and Medical Devices Agency to the Ombudsman questions on EMA pre-submission activites.

Best regards
Christa Wirthumer-Hoche

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AGES Gesundheit für Mensch, Tier und Pflanze

Responses to questions posed by the Ombudsman on EMA pre-submission activites

from the

Austrian Medicines and Medical Devices Agency

1. It may happen that EMA staff members and experts who participate in pre-submission activities will be involved in the subsequent *scientific evaluation and/or marketing authorisation* procedure for the same medicine.

To what extent is this a matter of concern, if at all? Are there specific pre-submission activities of particular concern in this regard? How should EMA manage such situations?

Answer AT:

Background: profound scientific knowledge, a high level of professionalism as well as consistency regarding the provided answers is expected by the applicant. With this regard the involvement of specific experts who already participated in pre-submission activities in the subsequent scientific evaluation and/or marketing authorisation procedure for the same medicine is beneficial.

Independent and consistent decision making is guaranteed by the following factors:

- the legally non-binding character of Scientific Advice
- quorum requirements at CHMP level
- strict requirements for assessors regarding declaration of interests
- involvement of relevant expert groups and working parties
- designation of Rapporteurs without involvement of medicine developers
- independent peer reviews
- transparent dialogue among EMA and member states
- correspondence with Applicants strictly via EMA

Therefore no further measures by EMA are considered required.

2. Should EMA allow experts from national authorities, who have previously provided scientific **advice** at national level on a particular medicine, to be involved in EMA's scientific **evaluation** of the same medicine?

   Answer AT:

   Yes (see responses to Q1).

3. What precautionary measures should EMA take to ensure that information and views provided by its staff members and experts in the context of pre-submission activities are not, in practice, considered as a "binding" pre-evaluation of data used to support a subsequent application for authorisation?

   Answer AT:

   - Regarding EMA scientific advice: It is laid down that a scientific advice is not legally binding with regard to any future marketing authorisation application of the product concerned, neither on the Agency/CHMP nor on the sponsor. This information could be provided to the sponsors/applicants in a more prominent/transparent manner.
   - The full extent and quality of the data as well as the final individual results of a development program for a medicinal product are usually not known at the stage of a request for scientific advice and therefore any recommendations made in scientific advice cannot pre-empt the outcome of the assessment of these data. Once the final set of data is available and submitted for a marketing authorisation application, they are taken into account in their entirety for a judgement of the benefit/risk balance, without being bound or limited by earlier scientific advice considerations.
   - Regarding Pre-submission Meetings: according to our understanding EMA expects advice primarily regarding structure of the dossier and only general scientific questions. There is never any kind of pre-assessment of data included. The non-binding character and purpose of these meetings should be clearly communicated to the applicants by EMA as well as by national authorities.

4. Is the way in which EMA engages with medicine developers in pre-submission activities sufficiently transparent?
   If you believe that greater transparency in pre-submission activities is necessary, how might greater transparency affect: i. EMA's operations (for example the efficiency of its procedures, or its ability to engage with medicine developers) and ii. medicine developers?

   Answer AT:

   In general, the engagement of EMA in pre-submission activities is considered sufficiently transparent.

5. Is there a need, in particular, to enhance the transparency of scientific advice EMA provides to medicine developers? Would it, in your opinion, be useful or harmful, for example, if EMA:
   - disclosed the names of the officials and experts involved in the procedures;

- disclosed the questions posed in scientific advice procedures; and/or
- made public comprehensive information on the advice given.

If you have other suggestions, for example regarding the timing of the publishing of information on scientific advice, please give details and the reasons for your suggestions.

Answer AT:

Disclosure of the names of the officials and experts involved in the procedures: disclosing the names of all experts involved in a specific procedure to the respective Applicant could be considered to increase transparency. Currently the names of the "officials involved" are actually disclosed, e.g. in all scientific advices the Coordinators and EMA project lead and in PIPs Paediatric Coordinator, Rapporteur and Peer Reviewer are included by name. Regarding the release of the information on the officials and experts involved to the general public: this would increase transparency, however such publication may also be critical, especially regarding experts for toxicology studies and questions related to animal experiments. Therefore, the benefit of publishing the experts' names is debatable.

Disclosure of questions posed in scientific advice procedures: this proposal is considered harmful since this transparency might lead to the apprehension by medicine developers that confidential and valuable information is published. This information is in addition not informative for the public. A decrease in submitted Scientific Advice requests could be the consequence.

Regarding the question of making public comprehensive information on the advice given the same considerations apply as expressed for the previous question, as long as the development program has not been finalised and the marketing authorisation application procedure has not been concluded. A more extensive description of the scientific advice recommendations could be considered at the stage of publication of the EPAR.

6. What would the advantages and disadvantages be of making scientific advice, given to one medicine developer, available to all medicine developers?

Answer AT:

Scientific Advice is given related to a context and not a cook-book exercise. The content depends on the Applicant's strategy and results obtained in previous steps and is not generalizable. Therefore, despite of existence of specific guidelines Applicants still request scientific advice.

However, in exceptional cases, broadly applicable advice might be provided as publicly accessible guidance documents e.g. focusing on regulatory procedural or legal aspects,

but also scientific consensus on specific indications, methods or products. In terms of format, the range spans from legal documents, over guidelines, reflection papers and simple Q&A documents to specific qualification opinions, which are a specialised format of scientific advice/conclusions given and are indeed made public on the EMA website.

7. Should EMA be limited to providing scientific advice only on questions not already addressed in its clinical efficacy and safety guidelines?

   Answer AT:

   No, scientific advice should provide the opportunity to raise all different kinds of scientific questions. A restriction is not considered useful since

   -guidelines are not binding, but address general development principles

   -such a limitation would hamper innovative approaches

   -the large value of scientific advices is that everybody is free to ask

   -commonly Applicants require advice although there are guidelines

   -every case is specific and deserves a separate handling. No size fits all

8. Any other suggestions on how EMA can improve its pre-submission activities? If so, please be as specific as possible.

   Answer AT:

   Over the last years a new trend regarding presubmission meetings was observed. Questions from the applicants do often not restrict to formal aspects (e.g. structure of the dossier or general high-level scientific aspects) but have the appearance of a more detailed scientific advice. A clearer definition regarding the content of presubmission meetings would be helpful.