[redacted]

From: [redacted]
Sent: 30 January 2019 13:34
To: EO-PresubmissionConsultation
Cc: [redacted]; Policy Intern
Subject: Public consultation on EMA pre-submission activities - CPME response
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Follow Up Flag: Follow up
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Dear Mr Roovers,

Please find attached the Standing Committee of European Doctors' (CPME) response to public consultation on how the EMA engages with medicine developers before they apply for authorisations to market their medicines in the EU.

Kind regards,
Carole Rouaud

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Senior Policy Adviser

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On 29 January 2019, the CPME Executive Committee adopted the 'CPME response to public consultation on how the EMA engages with medicine developers before they apply for authorisations to market their medicines in the EU' (CPME 2019/009 FINAL).

CPME response to public consultation on how the EMA engages with medicine developers before they apply for authorisations to market their medicines in the EU

INTRODUCTION

In 2017, the European Ombudsman opened an inquiry (OI/7/2017/KR) into the arrangements that the European Medicines Agency (EMA) has in place for engaging with individual medicine developers before they submit applications for authorisations to market their medicines in the EU (so-called 'pre-submission activities' or 'pre-authorisation activities'). Essentially, these 'activities' involve EMA providing advice, opportunities for dialogue and consultation, and regulatory and scientific support for medicine developers on different aspects of the authorisation process.

EMA's reply to the letter opening the inquiry, and a follow-up meeting, have given the Ombudsman a better understanding of the different types of pre-submission activities that exist. In so far as these activities facilitate the development and availability of high-quality, effective and safe medicines, they benefit patients and serve the public interest. Nonetheless, such meetings and preliminary discussions may pose some risks, including to the objectivity of how authorisation applications are subsequently assessed, particularly where the process is not sufficiently transparent.

CPME responses appear in Blue.

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How the European Medicines Agency engages with medicine producers before they apply for authorisations to market their medicines in the EU

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?**

Scientific advice can help both the medicine developers and regulators making sure that appropriate data and evidence are collected before the granting of a marketing authorisation, especially for new medicines.
Nevertheless, such advice should not bind regulators for their final decision. In this context, the involvement of a staff member or an expert at both pre-submission and marketing approval

levels could potentially lead to a bias in the final decision. Consequently, it is important that the final decision is taken according to the principle of collegiality and involves several experts, incl. some experts not involved in previous discussions with the medicine developers. Moreover, EMA staff members and experts involved in pre-submission activities should not take the function of rapporteur or co-rapporteur in the subsequent scientific evaluation and/or marketing authorization procedure.

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?

The same requirements as above should be applied. The scientific evaluation should be a collegial exercise which should involve several experts from different backgrounds. Nevertheless, given the limited number of experts in certain fields, regulators might have to rely on the same experts in certain cases. Similarly, the function of rapporteur or co-rapporteur should not be attributed to an expert who have previously provided scientific advice at national level on a particular medicine.

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?

It should be specified in the pre-submission file that any recommendations provided by EMA's staff members and/or experts is not legally binding and is taken on the basis of the most recent scientific knowledge. On the other hand, it implies that the medicine developers should also be free to follow or not the advice provided by EMA. Nevertheless, any divergence from the scientific advice should be justified.

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?

Greater transparency should be provided with respect to pre-submission activities and the final recommendations provided by EMA. A report of the scientific advice provided for a specific medicinal product should be made publicly available at the latest when the marketing authorisation is granted (alongside with the EPAR). A summary of all scientific advice activities performed by EMA should also be made regularly available to the public.

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.

See answer to question 4. The information asked for in the three bullet points should be given (i.e. alongside with the EPAR).

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

No comment.

7. Should EMA be limited to providing scientific advice only on questions not already addressed in its clinical efficacy and safety guidelines[4]?

Given that specific questions, especially regarding the design of clinical trials for specific medical conditions, cannot be answered in general "clinical efficacy and safety guidelines", early scientific discussion on all aspects of drug development, including trial design, can be valuable and should therefore be encouraged.

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

We should demand that, in addition to Health Technology Assessment (HTA) bodies and patient representatives, health care professionals (HCP) are involved in pre-submission activities, such as parallel regulatory-HTA scientific advice. Of course, all principles of the "Guidance for Parallel Consultation" (e.g. confidentiality, declaration of and correct handling of conflict of interest) should be applied.