

[REDACTED]

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**From:** [REDACTED]  
**Sent:** 18 December 2018 09:53  
**To:** EO-PresubmissionConsultation  
**Cc:** [REDACTED]  
**Subject:** Comments Ombudsman Inquiry on EMA pre-submission activities  
**Attachments:** 181218 EU Ombudsman EMA scientific advice comments GKVSV.PDF; 181218 EU Ombudsman EMA scientific advice comments GKVSV.DOCX

Dear Madame or Sir,

Thank you indeed for the opportunity to contribute to the Ombudsman's Inquiry on EMA pre-submission activities. Please find comments by the German National Association of Statutory Health Insurance Funds enclosed.

Please feel free to contact our expert, [REDACTED], or me in case you have any questions or comments.

Best regards,

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**Comments by the  
National Association of Statutory  
Health Insurance Funds  
from 18.12.2018**

**to the European Ombudsman's inquiry  
How the European Medicines Agency engages with medi-  
cine producers before they apply for authorisations to  
market their medicines in the EU  
OI/7/2017/KR**

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## I. Comments

- 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?**

Involvement in both, scientific advice and subsequent evaluation bears the risk of bias. It may well be that the assessor's view changes if he or she accompanied a company and a product over years. It may as well happen that assessors inappropriately bind themselves to a piece of advice that today seems outdated, when they know they have given this advice themselves in the past.

Due to this reason the European Parliament amended the Commission Proposal for a regulation of the European Parliament and of the Council on health technology assessment and amending Directive 2011/24/EU to ensure that the assessor and the co-assessor appointed to carry out the scientific advice shall not be the same as the assessor and co-assessor appointed for the joint technological assessment.

It is unclear to what extent this risk of bias has already materialised or will materialise in future. Special awareness seems necessary regarding the PRIME initiative, where one of the key features is the early appointment of a rapporteur responsible for the project beginning with early advice up to marketing authorisation.

In the view of guaranteeing a maximum of independency, this situation should be avoided whenever possible and advisory and assessment functions should be separated.

- 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?**

In principle the same reservations are applicable to experts from national authorities that apply to EMA staff and were pointed out in the answer to question 1.

- 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?**

Informal self-commitment is hard to address and avoid. EMA personnel needs to be aware of this risk and needs to reflect all of its decisions properly. In this reflection, a structured process for second opinions or rotation might be an advantage.

In addition, advised developers should be informed by means of a formal disclaimer that although information and views provided within EMA's advice are sound and reliable, in a view of possible changes e.g. in knowledge they still are to be considered non-binding.

**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?**

Currently, the pre-submission activities of EMA are not sufficiently transparent and should be amended accordingly. Only very limited information is publically available on the content and outcome of EMA scientific advice. In a first step, EMA should reassess current processes with the aim of identifying which parts of its pre-submission activities could be performed publicly. Especially for those questions, which are repeatedly discussed with different applicants, guidance documents and workshops could be an appropriate format. Confidential advice should be strictly confined to really commercially sensitive topics. Any advice given should be reevaluated at the time of marketing authorisation, whether its contents are still confidential. If possible, the content of EMA's advice should be published as an annex of the European Public Assessment Report.

Distinguishing between confidential and non-confidential advice should not only enhance transparency, it would also diminish duplication of work. In addition, it would enable EMA to set transparent, uniform standards for therapeutic areas and allow for public debate on scientific requirements for marketing authorisation. However, by preserving space for confidentiality in special issues, interests of developers can also be taken into account adequately. A publication of the content of advices would also allow for an evaluation of the success of advice and adherence to the advice by developers.

**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.**

In line with our answer to question 4 we see the need for more transparency in these issues. A publication of questions and EMA's answers during scientific advice should be published latest at the time of marketing authorisation.

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

As already pointed out in our previous answer to question 4 and fed by our experiences on scientific advice on national level, although there are components of advice that might be highly individual, a good proportion of questions are relevant to all developers or at least all developers working in the same field. Therefore, making those parts of scientific advice public would diminish duplication of work, would allow for setting transparent, uniform standards for therapeutic areas and would in the end result in more standardised clinical trials and thereby improve comparability of clinical evidence. One disadvantage might be that developers need to inform themselves more proactively on relevant EMA documents. Therefore it might be sensible to further allow for general guidance meetings with developers, e.g. workshops. These could also be performed in public.

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

It would probably not be feasible to restrict EMA in this way. Questions already addressed in EMA's guidelines may come up due to various reasons, be it a lack of preparation by the applicant or the need for further clarification. However, questions arising from a lack of preparation could be answered in advance in written form. If these questions come up during the advice, again there is no need for confidentiality.

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

None that have not already been mentioned above.