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Comments Ombudsman Inquiry on EMA pre-submission activities - OI/7/2017/KR

Dear Ms O'Reilly

Please find attached the comments of the European Social Insurance Platform, representing the statutory social insurances in Europe, to the public consultation launched by the European Ombudsman with regard to the pre-submisison activities of the European Medicines Agency (EMA).

We remain at your disposal for further information, should you require it.

Yours sincerely

Chris Dawson

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Brussels, 30 January 2019

Comments Ombudsman Inquiry OI/7/2017/KR on EMA pre-submission activities

Dear Ms O'Reilly

The European Social Insurance Platform (ESIP) welcomes the opportunity to respond to the questions you posed with regard to your enquiry (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'). Please find our answers to your questions below.

Question 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 1: This is a matter of concern when the individual is involved in the provision of **pre-submission scientific advice** as it carries the risk of bias one way or another in the evaluation and/or authorisation process. For example, an assessor's objectivity may be compromised if he or she has accompanied a company and a product over several years. In addition, an assessor may inappropriately bind him-/herself to a piece of advice that he/she gave in the past and that some years later is no longer relevant.

We should be aware of the risk with particular regard to the EMA's **PRIME initiative**, where a key feature is the early appointment of a rapporteur who is responsible for the whole project, from the early advice stage up to marketing authorisation. While this provides important benefits for the developer (greater efficiency, continuity, less ambiguity) it increases the risk of bias in the authorisation process.

Ensuring the independence of the evaluation and/or authorisation process requires **clear separation of the advisory and evaluation procedures as well as increased transparency.**

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Question 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 2: The same considerations are applicable to experts from national authorities as to EMA staff and are addressed in our answer to question 1.

Question 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 3: Informal self-commitment is hard to address and avoid. EMA staff and experts need to be aware of this risk and need to reflect carefully on their decisions.

The **involvement of a broader group of external experts/stakeholders in pre-submission activities** could help address this issue, along with the possibility for an internal request for **a second opinion**.

In addition, developers receiving advice from EMA should be informed by means of a **formal disclaimer** that the information given and the views expressed, while aimed to be sound and reliable at the time are nevertheless susceptible to changes e.g. in knowledge and should therefore always be considered non-binding.

Question 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 4: Currently, the **EMA's pre-submission activities are not sufficiently transparent** and this needs to be addressed. In particular, very limited information is publicly available on the content and outcome of **scientific advice** provided by EMA. EMA should reassess current processes with the aim of identifying which parts of its pre-submission activities could be made public. **For questions of common interest** to medicines developers that are repeatedly discussed with different applicants, **public guidance documents and workshops could be mutually beneficial**.

Confidential procedures should be strictly limited to truly commercially sensitive topics. At the time of marketing authorisation, advice given under terms of confidentiality should be re-evaluated to assess if the contents can still be considered confidential. Non-confidential advice should be published as an annex to the European Public Assessment Report.

Publishing non-commercially sensitive advice would not only enhance transparency but also diminish duplication of work. In addition, it would enable EMA to set transparent, uniform standards for different therapeutic areas and allow for public debate on the scientific requirements for marketing authorisation.

At the same time, **publication of the content of EMA's scientific advice would allow for an evaluation of the success of the advice process** and its usefulness to developers and downstream decision-makers.

Question 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 5: Yes, there is a need for more transparency regarding scientific advice given to developers (see Answer (to question) 4).

With view to greater transparency, **publishing the names of officials involved in scientific advice** should not be problematic and **should be encouraged**. In the case of experts, however, publication of their names may make them vulnerable to approach by external parties.

It would be useful to publish the questions posed and the advice given during scientific advice procedures as soon as possible and **at the time of marketing authorisation at the latest**. The accumulated knowledge and experience should be made publicly available for re-use by relevant stakeholders, research and society.

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

Answer 6: See answer (to question) 4. While there are components of scientific advice that might be highly specific to one developer, a large proportion of questions posed during scientific advice procedures are relevant to all developers or at least all developers working in the same therapeutic and/or technology field. **Making common elements of scientific advice available to all developers** (e.g. through guidance documents and workshops) **would 1) diminish duplication of work, and 2) allow for setting transparent, uniform standards for specific therapeutic areas, resulting in more standardised clinical trials and improved comparability of clinical evidence**.

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

Answer 7: **Strictly circumscribing scientific advice in this way may not be feasible**. An applicant may require further clarification around certain questions already addressed in EMA's guidelines. **Questions arising from a lack of preparation by the applicant**, however, **could be answered in advance in writing**.

Question 8: Any other suggestions on how EMA can improve its pre-submission activities?

Answer 8: **EMA should aim to involve the relevant stakeholders (patients, academia, healthcare professionals, HTA, payers) as soon as possible in its procedures** to avoid duplication of effort.

Further, the complexities and specificities of new and upcoming technologies will require **more proactive collaboration with and between existing experts** in the EU. EMA should work to develop such a collaborative approach.

Yours sincerely,

Arnaud Emériau,

ESIP President

About the European Social Insurance Platform (ESIP)

The European Social Insurance Platform (ESIP) represents over **50 national statutory social insurance organisations** in **16 EU Member States and Switzerland**, active in the field of health insurance, pensions, occupational disease and accident insurance, disability and rehabilitation, family benefits and unemployment insurance. The aims of ESIP and its members are to preserve high profile social security for Europe, to reinforce solidarity-based social insurance systems and to maintain European social protection quality. ESIP builds strategic alliances for developing common positions to influence the European debate and is a consultation forum for the European institutions and other multinational bodies active in the field of social security.