Letter from the European Ombudsman to the European Medicines Agency opening strategic inquiry OI/7/2017/KR into pre-submission activities organised by the Agency.

Correspondence - 17/07/2017
Case OI/7/2017/KR - **Opened on** 17/07/2017 - **Decision on** 17/07/2019 - **Institution concerned** European Medicines Agency (No further inquiries justified) |

Mr Guido Rasi

Executive Director

European Medicines Agency (EMA)

Strasbourg, 17/07/2017

Subject: Strategic inquiry into pre-submission activities organised by the European Medicines Agency (OI/7/2017/KR).

Dear Mr Rasi,

I have decided to conduct a strategic inquiry, on my own initiative, into the arrangements that the European Medicines Agency (EMA) has in place for engaging with individual medicine developers before the Agency receives applications for marketing authorisations from them ("pre-submission activities") [1] .

In so far as these activities help the development and availability of high-quality, effective and acceptably safe medicines, they benefit patients and serve the public interest.

Nonetheless, such activities may pose some risks, such as that the eventual decisions by EMA on the authorisation of medicines may be influenced by what has been discussed during the meetings with medicine developers prior to receiving their marketing authorisation application. I note that EMA sees pre-submission meetings as a way to *"enable medicine developers to establish contact with the Agency staff who will be involved with the application"* [2] .

Even if EMA were to ensure that its subsequent assessments of applications for marketing authorisations are objective and complete, there is still a risk that pre-submission activities create, in the eyes of the public, at least some perception of bias. [3] These risks must be

managed.

One way to do this is by ensuring that the process is sufficiently transparent. A preliminary assessment suggests that more could be done in this area.

As a first step, I would be grateful if a meeting could be arranged between my staff and your staff so that my Office can learn more about EMA's approach to pre-submission activities. The questions below will serve as the basis for that meeting.

As pre-submission activities appear to be central to the procedures related to accelerated marketing authorisation, including 'adaptive pathways' [4] and 'priority medicines' [5] , I would be grateful if EMA would take these procedures into account in its replies. In particular, I would be grateful if EMA would set out its specific approach to pre-submission activities concerning accelerated marketing authorisation procedures.

In replying to the following questions, please feel free to add any detail which may further my Office's understanding of these issues.

Concerning the overall framework that applies:

1. Which rules or regulations, including internal decisions, form the basis of EMA's current practice of organising pre-submission activities? Please provide copies (if available online, a link to the relevant page suffices).

2. When EMA receives a request for a pre-submission activity, how does it assess if the activity is likely to facilitate the achievement of EMA's own objectives and thus serve the public interest?

Regarding pre-submission activities themselves:

3. Please provide a list of key pre-submission activities EMA currently offers to medicine developers, briefly describing each activity and who, typically, participates in such pre-submission activities from EMA's side.

4. Please provide a statistical overview of pre-submission activities held from 2012-2016 with an indication of the type of pre-submission activity and the type of medicine developer involved (for example SMEs, large companies or applicants from the academic sector)? Please identify the 10 medicine developers EMA met with most frequently in the context of pre-submission activities during this period.

5. EMA's 'pre-authorisation procedural advice for users of the centralised procedure' [6] notes that medicine developers may meet with the relevant (co-)rapporteur [7] and assessment teams at the national level prior to submission. EMA further states that it wishes to stay informed about such activities. [8] Please provide a statistical overview of such activities from 2012-16 with an indication of the type of medicine developers that had such meetings (for example SMEs, large companies or applicants from the academic sector).

Please identify the 10 medicine developers that (co-)rapporteurs met with most frequently in the context of pre-submission activities during this period.

6. Does EMA charge medicine developers to cover the costs of preparing for and attending pre-submission activities as well as the costs of any follow-up? If so, are there separate charging arrangements for first-timers, applicants from the academic sector, SMEs or large companies?

7. Does EMA allow persons (EMA staff, coordinators, rapporteurs and/or co-rapporteurs) to participate in pre-submission activities on a product if they will have a significant role in EMA's subsequent scientific evaluation and/or marketing authorisation procedure for the same product? If so, please explain for each relevant activity why EMA feels this is necessary and appropriate?

8. Does EMA take precautionary measures to ensure that information and views provided by EMA in the context of pre-submission activities do not constitute a pre-evaluation of data to support a marketing authorisation application? If so, could you please describe, for each relevant activity, these measures?

On the transparency of pre-submission activities:

9. There is no basic information publicly available on pre-submission activities organised by EMA, for example categorised in aggregate format about the type of pre-submission activity or the type of medicine developer. Would EMA be willing to publish this information? If not, could you please explain why not?

10. Does EMA publish the detailed minutes of pre-submission meetings, including the detailed advice provided in pre-submission activities, at any stage, for example as an integral part of the European public assessment report? If not, please explain why not?

On a general note, and not related solely to pre-submission activities:

11. Please describe the rules EMA has in place to govern contacts between, on the one hand, staff, coordinators and rapporteurs, and, on the other hand, medicine developers that apply for marketing authorisation?

It would be helpful if the meeting could be organised to take place in September 2017. Should your staff require any further information or clarifications concerning the inquiry, they can contact my Strategic Inquiries Unit (Mr Koen Roovers, email: koen.roovers@ombudsman.europa.eu , tel: +32 228 41 141).

Yours sincerely,

Emily O' Reilly

European Ombudsman

[1] To date, I am aware of “pre-submission meetings”, “regulatory strategy meetings” and “scientific advice meetings” as activities that might fall within the scope of ”pre-submission activities”. There may be other activities coming within this definition.

[2] For a description of pre-submission meetings, see for example: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000179.jsp&r

[3] A specific example of this general concern can be found in the contribution of the European Consumers Organisation (BEUC) to the European Food Safety Authority’s public consultation on ‘Open EFSA’: http://www.beuc.eu/publications/beuc-x-2014-077_ipa_open_efsa-beuc_response_to_the_public_consulta I also took note of a press release issued by a company when it submitted its application for a marketing authorisation. The company deemed the interactions it had had in advance of the application with its appointed Rapporteurs to be sufficiently important to report publicly as potentially making a difference, specifically the point that – according to the company - the Rapporteurs signaled support for the application.

[4] http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000601.jsp&r

[5] http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000660.jsp&r

[6] http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/1 .

[7] A rapporteur, and if relevant a co-rapporteur, is appointed to coordinate and assess scientific evaluations that EMA carries out. Rapporteurs and co-rapporteurs are tasked to provide objective scientific opinions. For more information, see: http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/1

[8] http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/1 , see page 48.