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From: [REDACTED]
Sent: 30 January 2019 16:09
To: EO-PresubmissionConsultation
Subject: Comments Ombudsman Inquiry on EMA pre-submission activities
Attachments: Bayer Comments Ombudsman inquiry on EMAs presubmission activities.pdf

Follow Up Flag: ema3
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Dear Sir or Madam,

Please see the attached letter re. Ombudsman Inquiry on EMA pre-submission activities.

Please do not hesitate to contact me in case of questions.

Sincerely,
Cathrine Schmidt

Freundliche Grüße / Best regards,

Dr. Cathrine Schmidt
Sr. Manager, Reg. Policy & Intelligence

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Bayer AG
Research & Development, Pharmaceuticals
Regulatory Intelligence
Building M085, 123
13353 Berlin, Germany
Tel: +49 30 468-1 [REDACTED]
Mobile: +49 [REDACTED]
E-mail [REDACTED]
Web: <http://www.bayer.com>
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/// Vorstand: Werner Baumann, Vorsitzender | Liam Condon, Hartmut Klusik, Kemal Malik, Wolfgang Nickl, Stefan Oelrich, Heiko Schipper
/// Vorsitzender des Aufsichtsrats: Werner Wenning
/// Sitz der Gesellschaft: Leverkusen | Amtsgericht Köln, HRB 48248



Submission via email to

EO-PresubmissionConsultation@ombudsman.europa.eu

European Ombudsman
1 avenue du Président Robert Schuman
CS 30403 F-67001 Strasbourg Cedex
France

Re: Comments Ombudsman Inquiry on EMA pre-submission activities

Dear Sir or Madam,

Reference is made to "How the European Medicines Agency engages with medicine producers before they apply for authorisations to market their medicines in the EU - Invitation to comment within the European Ombudsman's inquiry OI/7/2017/KR", published 8. October 2018. Bayer is pleased to submit comments to the published questions.

Bayer is a Life Science company with a more than 150-year history and core competencies in the areas of health care and agriculture. With our innovative products, we are contributing to finding solutions to some of the major challenges of our time. With life expectancy continuing to rise, we improve quality of life for a growing population by focusing our research and development activities on preventing, alleviating and treating diseases.

We thank you for your consideration of our comments to your questions. If you have any questions, please do not hesitate to contact me by phone at +49 202 36 [REDACTED] or via e-mail at [REDACTED]

Sincerely,

[REDACTED]
Dr. Isabelle Stöckert
Head Regulatory Affairs Europe, Middle East & Africa



January 28, 2019

Dr. Isabelle Stöckert

Bayer AG
Pharmaceuticals, Development
Regulatory Affairs

Aprather Weg 18 a
42113 Wuppertal
Germany

Tel. +49 202 36 [REDACTED]

www.bayer.com

Board of Management:
Werner Baumann, Chairman
Liam Condon
Hartmut Klusik
Kemal Malik
Wolfgang Nickl
Stefan Oelrich
Heiko Schipper

Chairman of the
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Werner Wenning

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Leverkusen
Local Court of Cologne
HRB 48248



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Strategic inquiry into pre-submission activities organised by the European Medicines Agency (OI/7/2017/KR) - Bayer Response to EU Ombudsman

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?

This should not be a concern for any type of pre-submission activity, quite the reverse. Through earlier engagement the individuals are more familiar with the product and its technology and are better able to identify critical issues and so ensure the benefit/ risk assessment is correctly focused.

Further, in view of the fact that there are adequate measures in place within the EMA, including a strict policy for managing conflicts of interest, a well-established process for independent evaluation of medicines and a high level of transparency of the EMA's operations including meeting conduct, we do not consider that EMA staff and experts who may be involved in both pre-submission activities and marketing authorization procedures for the same product is a particular concern.

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?

We believe that there is no conflict or risk to the integrity of the evaluation when using the same expert at national as well as EMA level. This brings the benefit of consistency in the advice by EU Regulatory Authorities on development of a product.

The experts involved in EMA's scientific evaluation of a medicine have been accredited as European experts. These experts are bound by EMA's policy on handling declarations of interests for scientific committee



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members and experts and, as such, part of the adequate measures mentioned under 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?

These measures exist and are already clear and understood in any advice delivered by the EMA.

EMA presently executes a variety of measures to ensure that its pre-submission activities, including scientific advice, are not explicitly or implicitly perceived as “binding” for or “pre-evaluations” of consequent Marketing Authorisation Applications. On its webpage, EMA states, “Scientific advice received from the Agency is not legally binding on the Agency or on the medicine developer with regard to any future Marketing Authorisation Applications for the medicine concerned”.

Additionally, as referenced on the webpage, scientific advice is offered as an optional opportunity for a company to seek essential input on key research questions and the overall merits of its development plans. Scientific advice is not an interaction directly between the company and one individual regulator– i.e., scientific advice is not a one-to-one engagement. Multiple regulators (e.g., EMA staff, CHMP/CVMP members, Rapporteurs) participate in scientific advice.

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?

In our opinion the way which EMA engages with medicine developers in pre-submission activities is sufficiently transparent. Such transparency becomes relevant for the public for those products that are approved. Elements of any scientific advice given might be discussed in European



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Public Assessment Reports (EPARs) and/or in the case of human medicines Module 2 documents published under Policy 0070 as Scientific Advices are part of the approval dossier. Furthermore, in accordance with European Union (EU) law, 3rd parties can request access to such scientific advice through the EMA policy on access to documents, POLICY/0043 and these documents can be released once the decision making is complete on a particular product for which the scientific advice was sought.

Further increase in the level of transparency would lead to information on future applications being made public before the application is submitted and approved and would deter medicine developers from having very detailed discussions with the regulators at this early stage. This could have a detrimental impact on the development of medicines leading to inefficiencies in the process which could also adversely impact patients, sick animals and even the wider 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.

We believe that the current procedures are fit for purpose. The existing EMA approach of the use of accredited EU experts to provide scientific and technical expertise with the assessment conducted at Committee level, where names, details and curriculum vitae of all committee members are available, ensures a robust and transparent advice process.

Disclosure of questions or comprehensive summaries made publicly available will provide major competitive disadvantage not only in terms of market access but especially with potential intellectual property transfer to the public.



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When there are recurring themes, across more than one developer, on questions posed for scientific advice, the EMA takes these into consideration as a trigger to develop new guidance or revise existing guidance. The revision of guidance or development of new guidance is done in a transparent manner with drafts released for public consultation and where the proposed new guidance is significant, a workshop with multiple stakeholders may be held. Such new or revised scientific guidance does not relate to advice that an individual company sought but rather to advice across multiple developers.

Further, as mentioned in question 4, 3rd parties can request access to any scientific advice document through European Medicines Agency policy on access to documents, POLICY/0043.

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

Scientific advice is always specific to one product and the advice may not be pertinent to another albeit similar product. Scientific advice is sought usually on particular aspects of development of a medicine not the entirety of development.

The proposal above would lead to disclosing proprietary information and withhold medicine developers continue to engage in these important scientific advice procedures in Europe, as discussed above. Advice in other jurisdiction would still be sought and would then solely drive development of new innovative medicines. In case advice has wider and general applicability then this can be managed through the development and issue of guidelines.

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

EMA should not be limited to providing scientific advice only on questions not already addressed in its clinical efficacy and safety guidelines. Given the complexity of drug development guidelines may still permit alternative approaches to be used if scientifically sound and justified. It is exactly such approaches that should be open to scientific advice.



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Furthermore, guidelines can be subject to different interpretations and so in cases of doubt it is important to understand the regulators' interpretation in the context of a specific product before designing and conducting studies. An important benefit of scientific advice is therefore to allow proactive discussions between regulators and medicine developers of proposed deviations from guidelines and their potential regulatory acceptability given the specific characteristics of the compound. Limiting the provision of scientific advice to questions not already addressed in EMA guidelines would prevent these important discussions thereby leading to potential limitations in drug development.

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

The EMA response to the Strategic Inquiry into pre-submission activities organised by the European Medicines Agency (EMA/566402/2017) outlined the key benefits of pre-submission activities with medicines developers. Primarily (in summary):

- Facilitates the elaboration of product developments plans that address regulatory requirements which can ultimately lead to more efficient development of products and provide patients with timely access to new, safe effective medicines.
- Protect patients and maximise the value of their involvement in clinical trials.
- Gain an overview of the product and development and understand what is coming through the pipelines.

It is crucial that these activities continue to ensure that companies of all sizes receive the necessary advice to achieve the above.